The Australian and New Zealand
JOURNAL OF SURGERY

Vol. XXII—No. 2 NOVEMBER, 1952.

SURGERY OF THE LARYNGO-PHARYNX AND CERVICAL OESOPHAGUS

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CARCINOMATA of the laryngo-pharynx and cervical oesophagus are usually fatal in outcome, and are associated with an appalling distress which excites surgical compassion.

Simpson (1948) quotes the 1945 Report of the Clinical Research Committee of the British Empire Cancer Campaign with records of 384 cases of laryngo-pharyngeal cancer, of which only 19 survived the five year period, and also the figures of the Holt Radium Institute (1946) referring to 220 patients of which 9 survived for five years.

The extirpative surgery of the region is fraught with great difficulties. The pathological processes are frequently formidable in local extent and lymph node metastasis frequent. Surgical interventions of great magnitude may be necessary, and in the past were carried out under conditions of imperfect anaesthesia and menaced by grave post-operative sepsis.

The lower pharynx and oesophagus present little vertical mobility, so that mobilization and suture, following excision, are rarely practicable.

The intimate association of the lower pharynx and larynx frequently dictate the removal of this latter important structure. Whilst the sacrifice of the larynx is no great price to pay for the cure of a lesion of such gravity, it requires considerable fortitude on the part of the patient to contend in addition with a fistula of the pharynx. Nevertheless, the plastic procedures for closure of a large post-operative pharyngeal fistula may involve the passage of considerable time, and when lymph node metastasis or grave local spread of malignancy has occurred they may never be completed.

The justification of mutilating surgery is the absence of a satisfactory alternative, but it can only be faced with equanimity when attended by a low operative mortality, and reasonable prospects of alleviation or cure. The former condition now obtains, but there are cases so advanced when they first seek aid that cure is out of the question even by the most radical methods of excision. Only time will show whether more recently introduced methods represent worthwhile alleviation in these cases.

Meantime, the position remains substantially the same as when Trotter stated: "No matter what may be our hopes about the discovery in the treatment of malignant disease of methods more specific and less harsh, surgical operation must be admitted to be the most useful and trustworthy means we now possess." (Quoted by Orton, 1951.)

MATERIAL

The material for this paper is derived from 25 patients referred for consideration of surgical treatment. The writer is a general surgeon with an interest in problems of oesophageal and pharyngeal surgery, and is indebted to Ear, Nose and Throat surgical colleagues who have referred cases, and

given invaluable assistance. In general, the type of case referred has been such that only very radical procedures would serve, and in most cases radiotherapy had either been already tried, or deliberately rejected as a therapeutic method. Owing to a special personal interest in the surgical relief of gross dysphagia, the 14 patients with lesions of the lower laryngo-pharynx (hypopharynx or post-cricoid) and cervical oesophagus bear a disproportionate numerical relationship to the more common growths of the upper laryngo-pharynx (epilaryngeal), for example, Fig. XXIII, of which there were 11 patients. Moreover, whilst a number of patients requiring total laryngectomy for intrinsic carcinomata of the larynx have not been included, the latter total includes 4 patients in which carcinomata arising primarily within the larynx, have belatedly spread from out the confines of the larynx to involve pharyngeal and other structures.

Age

The patients have nearly all been elderly and gravely debilitated. The youngest was aged 39 years, and the eldest 89 years, average 62 years. Those with growths in the lower laryngo-pharynx were of a later age group, averaging 65 years, whilst those in the upper laryngo-pharynx averaged 60 years.

Sex

The general trend in sex incidence is followed by this small series. Post-cricoid carcinoma predominates in females (11 females to 3 males in this group), and epilaryngeal carcinoma usually afflicts males (9 males to 2 females). This incidence was underlined remarkably by Pilcher (1948) in recording 100 consecutive cases at University College Hospital.

Epilaryngeal.	71 patients.	70 men. 1 woman.
Post-cricoid.	29 patients.	All women.

There is, however, an obvious difficulty in stating the site of some advanced tumours, which are seen late, at a stage when they may, for example, extend from the oropharynx to the thoracic oesophagus (Fig. XIX).

HISTORICAL

Czerny (1877) performed the first resection of the cervical oesophagus upon a patient suffering from a carcinoma who survived for fifteen months. Anatomical continuity was not restored.

The first excision of the cervical oesophagus followed by plastic reconstruction was achieved by Mikulicz (1866). His patient also died of a recurrence sixteen months later. De Quervain (1899) collected from the literature records of 14 similar operations attended by 5 operative deaths. All the survivors of operations died ultimately of recurrence.

Von Hacker (1908) reported the first successful excision of the cervical oesophagus and lower pharynx along with the larynx and upper trachea. His patient had survived this more radical procedure for eighteen months without recurrence.

Trotter (1913, 1931) contributed richly to the surgery of the pharynx and to the development of skin flap reconstruction operations.

Colledge (1943) was able to report results of surgery which have not been excelled. Of 39 patients subjected to lateral pharyngotomy, 13 (33 per cent.) were well ten years later, and of 16 patients treated by the more drastic method of pharyngo-laryngectomy, 6 (37 per cent.) were alive without recurrence after the same period.

Wookey (1948) extended the scope of drastic excision and reconstruction methods.

Sweet (1948) and Garlock (1948) demonstrated the possibility of anastomosis of the stomach to the cervical oesophagus, or even the pharynx.

Rob and Bateman (1949) described a method of bridging gaps in the cervical oesophagus with tantalum gauze covered by fascia lata, and some work has been done by Rob (1951) and Negus (1951) to explore the possibility of primary reconstruction of the pharynx by buried polythene tubing covered by a skin graft.

MISCONCEPTIONS

Some misconceptions merit attention.

The first of these is that major surgical intervention in this region is still attended with a very high mortality. With improved anaesthetic and resuscitation methods, and chemotherapy, this is far from being the case.

In the various operations associated with 20 radical excisions of this series, only one death occurred, due to bronchopneumonia in a gravely debilitated patient, a month after operation. The neck tissues were so devitalized by deep X-ray that the wound broke down about the tracheotomy opening.

Many consider that the removal of the larynx produces intolerable disability. This is very far from the truth, in that patients of very low intelligence can rapidly master the use of an artificial larynx, and many patients with intelligent application, and the aid of a speech therapist, can acquire a pharyngeal voice which renders their disability slight. This is not to be confused with the semi-articulate belching speech referred to as oesophageal. It requires emphasis that a carcinoma in this region all too frequently involves the respiratory passages with disastrous obstruction and voice loss. A tracheotomy affords very incomplete relief when carried out below a florid malignancy productive of profuse, foul discharges, and the combination of gastrostomy and tracheotomy is scarcely tolerable.

Perhaps the greatest misconception is that the indiscriminate application of irradiation methods is preferable to surgery. There is almost universal agreement concerning the wisdom of irradiation of naso-pharyngeal malignancies, and most surgeons give pride of place to radiotherapy for growths of the oro-pharynx where surgery is suitably relegated to treatment of the lymphatic fields, and to growths which resist such therapy or recur.

In the case of the laryngo-pharynx, radiotherapy is attended with some success in the region of the epiglottis, but cure or extension of life is very rare in the case of malignant tumours of the pyriform fossa or lateral pharyngeal wall, and is almost never effected in post-cricoid and cervical oesophageal growths.

PATHOLOGY

The great majority of malignant growths of the laryngo-pharynx and cervical oesophagus are squamous-celled carcinomata with varying cell differentiation, and these constitute the only type encountered in the writer's series.

The radio-sensitive lympho-epithelioma which is not infrequent in the naso-pharynx and oro-pharynx is rare in the laryngo-pharynx, and extremely rare in the oesophagus. Willis (1947) stated that lympho-epithelioma did not occur in the last named structure but the writer has encountered the condition once in the lower oesophagus (Dunlop, 1950).

The association of chronic hypopharyngitis and iron deficiency anaemia (Paterson-Brown-Kelly syndrome of English writers or the Plummer Vinson syndrome of American writers) with post-cricoid carcinoma has been stressed by several authorities: Ahlbom (1936), Negus (1950), Simpson (1939) and Owen (1950). Both these conditions are usually met with in the female.

Pilcher (1948) has stressed the fact that early lymph node metastasis is more common with epilaryngeal than post-cricoid growths, and the writer is in agreement. Operations for the former are therefore suitably accompanied by lymph node dissection.

Cancers of the epiglottis and aryepiglottic folds are nearly always bulky and cervical metastases from the epiglottis are often bilateral.

Wookey (1948) reported that of 70 patients who died in Toronto General Hospital from cancer of the oesophagus and hypopharynx, 22 per cent. had no metastases and 16 per cent. were associated with regional lymph nodes alone. In this series 25 per cent. of patients appeared to be free of metastases on first presenting but some of these had grave local extensions. One case developed a late bone metastasis to the body of the humerus causing pathological fracture.

SYMPTOMATOLOGY

The onset is often insidious and the patient may be late in seeking treatment. The early symptoms may be little more than a slight discomfort, pricking sensation, or soreness in the throat. This has on occasion led to a fruitless tonsillectomy.

Minor changes in the voice, such as huskiness or a muffled tone may be significant. The back of the larynx may be fairly extensively involved in post-cricoid growths without much voice change.

Growths of the lower laryngo-pharynx and upper oesophageal growths are associated with dysphagia, but it is quite remarkable how gross the stenosis may become before the patient is driven to seek assistance.

This is particularly the case where such growths arise in patients who have long suffered from a chronic hypo-pharyngitis, who state they have "always had a small swallow."

Enlarged lymph nodes in the neck may be the first melancholy symptom, particularly in growths of the pyriform fossae.

DIAGNOSIS

This is most frequently made by the otorhino-laryngologist. Indirect or direct pharyngoscopy forms the most useful service. In any suspicious case a biopsy snipping is of great value, and direct pharyngoscopy is essential.

Straight X-ray examination may reveal displacement forward of the larynx or trachea. A barium swallow gives most assistance in the post-cricoid region and cervical oesophagus.

Bronchoscopy may be useful to detect invasion of the trachea and larynx.

THE CHOICE BETWEEN SURGERY AND RADIOTHERAPY

Radiotherapy does not offer very much prospect of cure for hypopharyngeal and cervical oesophageal growths.

McWhirter (quoted by Graham, 1942) treated 46 cases, of which not one survived three years, and many derived not even temporary relief. Rob (1951) records that of patients so treated at St. Thomas's Hospital, 31 cases of carcinoma of the hypopharynx and cervical oesophagus, average length of survival 6.1 months, of which the longest was one year and six months.

This writer states: "A review of the literature reveals several long term survivals after surgical excision, including: Graham (1942) 2 patients, 15 and 23 years respectively. Trotter quoted by Pilcher (1937) 1 patient, 10 years. Evans (1933) 1 patient, 23 years; Colledge (1945) 3 patients, 8, 9 and 12 years; and Owen (1950) 2 patients for more than 5 years. On the other hand I can find the records of only 3 patients who have survived for more than 5 years after radiotherapy; they are: Nielsen (1940) 1 patient, 6 years; and Watson and Pool (1948) 2 patients, both for more than 10 years."

It is, however, fair to say that at the junctional region — upper laryngo-pharynx (or epilaryngeal) growths present more favourable response to radiotherapy, especially when applied to growths which are superficial and not deeply infiltrating.

Lenz (1947) reported 28 cases of carcinoma of the epiglottis, in which metastases were present in 21. Nine patients survived for over five years.

Harris (1948) recorded 9 patients with carcinoma of the epiglottis, with 6 five-year cures.

Orton (1951) states that growths of the aryepiglottic fold differ with location. Those nearest the epiglottis tend to respond like epiglottic lesions whilst those near the arytenoid have a poorer outlook but are more favourable than those of the pyriform sinus.

Surgery is certainly preferable for growths of the hypopharynx and cervical oesophagus, and for growths which have invaded the cartilaginous structures of the larynx.

Where still practicable it should be employed for radio resistant cases and for recurrence after radiotherapy.

If an adequate course of radiotherapy has not resulted in complete disappearance of the cancer, this will not be achieved by a second course.

OPERATIVE TREATMENT

It is proposed to illustrate some of the methods available by reference to actual cases in this series.

I. Major Excision not possible

6 patients. 2 Preliminary gastrostomy. Exploration of the neck. Deep X-ray therapy (ineffective).

1 Souttar's intubation. Deep X-ray therapy (ineffective).

2 Deep X-ray therapy only. (One patient derived benefit. Both had grave local spread and extensive metastases).

1 Refused all treatment though considered operable.

II. Major Excisions

20 (one operation was for recurrence).

A. Total laryngectomy, plus partial pharyngectomy.

9 patients. 5 Epilaryngeal carcinomata.

4 Intrinsic carcinomata of the larynx with late spread to the pharynx. (In one case laryngectomy had been carried out and there was recurrence in the tracheal stump with involvement of the pharynx.)

B. Partial Pharyngectomy and oesophagectomy conserving the larynx.

2 patients. 1 Excision and primary reconstruction by suture.

1 Excision employing a large skin flap for primary reconstruction.

C. Pharyngo-laryngectomy and partial oesophagectomy.

8 patients. *5 Subsequent reconstruction of skin pharynx completed.

2 Reconstruction never completed.

1 Primary reconstruction of pharynx with polythene tube and skin graft.

*One patient had a further resection and reconstruction.

PRE-OPERATIVE TREATMENT

Meticulous attention must be given to dehydration, malnutrition, anaemia, and sepsis. Intravenous therapy is frequently required. Where the patient is able to swallow a semi-fluid diet rich in caloric value, proteins and vitamins should be given for a few days at least.

Gross mouth sepsis requires attention, and chemotherapy may reduce the toxicity and inflammatory oedema.

A preliminary gastrostomy is considered wise if a major reconstruction in stages is contemplated. These patients usually have lesions in the post-cricoid region, and lower oesophagus.

Preliminary tracheotomy is reserved purely for cases in which respiratory obstruction is grave and urgent. These cases usually have growths arising partly within the larynx.

Preliminary tracheotomy, however, disturbs the tissue planes and produces some infection, so that in most cases it is considered preferable to expose the trachea with the aid of local anaesthesia and then introduce a cuffed tube in the trachea, so that the major excision may be carried out with general anaesthesia.

ILLUSTRATIVE OPERATIVE CASES

Intubation to Relieve Dysphagia

Case 11

S.J.W., aged 89, a business man, presented with a history of sore throat, and progressive difficulty in swallowing over six weeks. This was now practically complete and he was troubled by the collection of foul saliva and an irritable cough. His voice was a little husky.

Examination and investigation revealed an extensive carcinoma behind the larynx, extending well down the cervical oesophagus. There were extensive glandular deposits with some fixation on both sides of the neck. He was very averse to a gastrostomy. On 28th April, 1951, the malignant stricture was dilated and a large Souttar's tube placed in position. This gave a deal of relief of his dysphagia, and he was not conscious of the tube.

Deep X-ray therapy did not have any effect. He slowly developed stridor and respiratory infection and died in two months.

Comment

This procedure represented merely a palliative gesture. A suitable moulded polythene tube would probably have been better.

Total Laryngectomy Plus Partial Pharyngectomy

Case 19

Mrs. E.B., aged 64 years, referred by Mr. Heyworth Watson, 15th February, 1950, complaining that for thirteen months she had had soreness of the throat and a pain in the right side of the neck, radiating to the right ear. She had felt a lump in the right side of the neck. She had developed slight difficulty in swallowing. Deep X-ray therapy was carried out seven months previously with disappearance of the palpable lump, but, after a short period of relief, pain and dysphagia had recurred. She was in poor general condition, and examination confirmed the presence of an extensive squamous celled carcinoma involving the epiglottis and the right pyriform fossa. Thickening was felt in the neck at the site of irradiated lymph nodes.

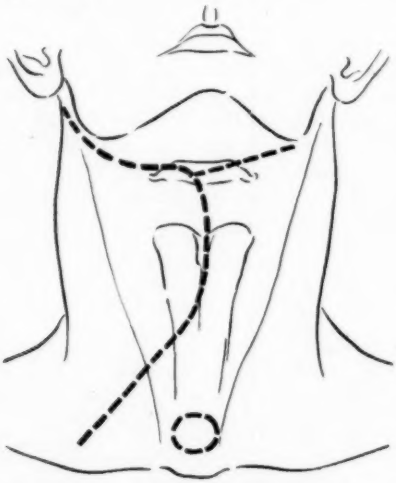

FIG. I. Diagram showing the anterior aspect of the neck; the dotted line represents author's incision, which permits excellent approach to the larynx and pharynx and radical block dissection of lymph nodes.

Operation on 23rd February, 1950. Under general intra-tracheal anaesthesia, a curved incision was made from the right mastoid process under the angle of the jaw just across the midline then curving back to the clavicle. A horizontal extension to the left under the chin was added (Figs. I and II). Skin flaps were resected, and a radical lymph node dissection carried out removing the anterior belly of the digastric muscle, the submandibular gland, the sternomastoid muscle, the jugular vein and the lower pole of the parotid gland, along with all fatty tissue and lymph nodes.

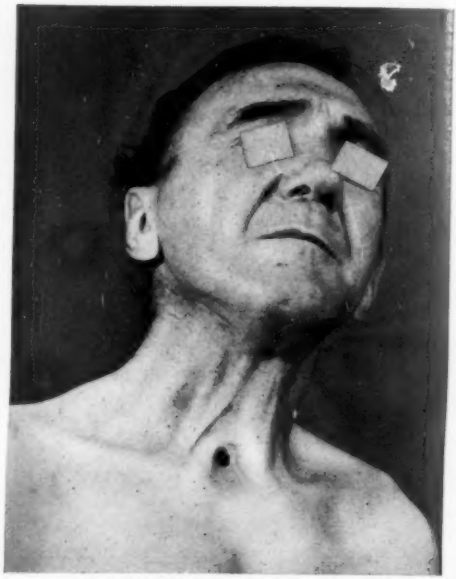

FIG. II. Photograph of patient showing the appearance following laryngectomy, partial pharyngectomy and radical lymph node dissection with this incision.

The external maxillary, lingual, superior thyroid and sternomastoid branches of the external carotid artery were divided. The right side of the hyoid bone was excised.

The pharynx was now opened through the thyreohoid membrane, the epiglottis hooked out and the tumour inspected. The larynx was then "skeletonized" by dividing the infra-hyoid muscles and the superior laryngeal vessels and nerves divided and ligated.

The attachment of the pharyngeal constrictors to the larynx was then divided. The trachea was divided obliquely below the third ring and a fresh, sterile cuffed tube inserted in the tracheal stump. The larynx was then dissected upwards towards the arytenoids dividing the recurrent laryngeal nerves and ligating the crico-thyreoid arteries. As much mucosa as possible was saved from the left side in the region of the pyriform fossa, but on the right side the lateral wall of the pharynx, pyriform fossa, and mucosa at the base of the tongue were excised with the epiglottis (Fig. III).

The pharynx was then reconstructed with chromic catgut, leaving a fairly roomy tube. The divided constrictor muscles and thyroid gland were sutured

FIG. III. Photograph of the specimen (posterior view) of excised larynx and portion of the pharynx, Case 19. Carcinoma involving epiglottis and pyriform fossa.

FIG. IV. Photograph of patient, from whom specimen shown in Fig. III was removed, employing artificial larynx.

across the line of pharyngeal closure. The wound was closed with drainage and the trachea sutured to the margins of a circular area of excised skin.

Progress

Wound healing was a little slow. There was no leakage. Swallowing was commenced in one week and has continued without disability. The gastrostomy opening closed spontaneously. The patient gained 2 stone in weight and remains well with no evidence of recurrence, and is active in her duties as a housewife (Fig. IV).

Case 23

Mr. W.C., aged 70. A case of advanced intrinsic carcinoma of the larynx with involvement of the arytenoid region and right pyriform fossa. The growth had invaded the wall of the larynx to reach the jugular vein and had infiltrated the right lobe of the thyroid. Enlarged lymph nodes were conspicuous (Fig. V).

An endoscopic operation had been performed on the right vocal cord in Scotland ten years before. He had had only a whisper since that event, and recently he had become very breathless and troubled by foul saliva. He had lost much weight.

FIG. V. Photograph of a sagittal section of larynx, Case 23. Intrinsic carcinoma of the larynx with extension to pharynx.

The operative procedure on 24th October, 1950, was similar to the above, except that a large U-shaped incision based on the chin was employed, and that the preliminary intubation of the trachea

was carried out operatively with local anaesthetic. It was necessary to excise the right lobe of the thyroid gland.

Progress

He healed well without leakage, gained 2 stone in weight, and acquired a good pharyngeal voice. Despite the unfavourable omens he has remained well for 18 months with no evidence of recurrence.

Invasion of the Trachea

Case 18

Mr W.E..B., aged 39, referred by Mr. E. Gutteridge, had suffered from an intrinsic carcinoma of the larynx for two years and nine months. This eventually spread out to the pharynx and down the trachea for 1½ inches. Deep X-ray proved ineffective. Necrotic cartilage sloughed out the front of the neck. A tracheotomy was necessary and was carried out six months previously. He still had great distress with his breathing.

On 23rd August, 1949, the larynx and involved pharynx and trachea were excised. The pharynx was primarily reconstructed and closed (with only slight temporary leak).

To secure skin junction with the trachea, a large Estlander flap was raised from the chest and rotated so that it could be sewn round the open end which then retreated into the thoracic cavity followed by a funnel of skin.

Progress

Rapidly developing lymphatic metastases required a block dissection on the right side of the neck on 7th December, 1949. Further metastases caused death a year after the first operation. The tracheal opening functioned perfectly throughout.

FIG. VI. Intrinsic carcinoma of the larynx with extension to pharynx. Diagram of the neck showing skin flaps rotated down to the stump of trachea following excision of a recurrence after laryngectomy.

Case 25

Mr. E.M., aged 62. Recurrence in the tracheal stump with slight involvement of the pharynx. Portion of the trachea was excised on 6th April, 1949, and the pharynx resutured after resection of a small portion. Skin flaps from either side of a vertical incision were rotated and sewn to the tracheal stump before allowing it to recede into the chest (Fig. VI). Split skin grafts were applied to the bare areas.

Healing and function were satisfactory. The patient died of coronary occlusion three months later.

Partial Pharyngectomy and Oesophagectomy, Conserving the Larynx

Case 9

Mrs. R.Y., aged 66, early post-cricoid carcinoma. This lady had suffered for approximately two years from discomfort and burning in the throat. An early barium swallow and oesophagoscopy failed to account for her symptoms. For a year there had been progressive dysphagia until she could swallow only fluids. Oesophagoscopy by Mr. T. G. Swinburne revealed a small fungating squamous celled carcinoma mainly on the posterior wall in the post-cricoid region.

Operation was carried out under general anaesthesia administered by Dr. Gordon Stanton on 4th March, 1950. The extensive incision employed in Case 19 (Fig. I) was employed. A radical block dissection of lymph nodes, along with the sternomastoid muscle and jugular vein, was carried out. The infra-hyoid muscles were removed on the right side, and the right half of the hyoid bone. The hypoglossal nerve on this side was inadvertently partly divided, and sutured. The superior thyroid, external maxillary and inferior thyroid arteries were ligated. The superior and recurrent laryngeal nerves were dissected carefully. The thyroid lobe was used as a tractor to rotate the larynx and the constrictor muscles were divided, giving free exposure of the pharynx and oesophagus. The tumour could be felt through the wall. The pharynx was opened above, and a sessile tumour was seen, the size of a bean, in the immediate vicinity of the cricoid. Only mucosa was involved, and there were two small horns of infiltration extending round each side, directed anteriorily to the back of the larynx.

A complete ring of pharynx and oesophagus was excised; commencing the excision to the left side, and suturing as the excision proceeded with interrupted sutures of fine chromic catgut tied with the knot on the mucosa. A Rehfuss tube was passed by the anaesthetist before the suture was completed. The pharyngeal muscles were sutured and the wound closed with drainage.

On section the lymph nodes were not involved.

Progress

She made an uneventful recovery and swallowed well after 5 days of tube feeding. She remains extremely well more than two years later, but the hypoglossal weakness has not fully recovered and leads to clumsiness with the lower denture.

Comment

The writer has not read an account of a ring excision in this region with primary suture and the opportunity must rarely present.

Case 2

Mrs. C.W., aged 65, suffering from a post-cricoid carcinoma, was first seen by me on 23rd September, 1948. She had suffered from dysphagia for nine months. Heavy irradiation four months before had not given much relief, and the obstruction was now almost complete. She was extremely wasted and ill.

The section of a biopsy specimen was reported as epidermoid carcinoma of squamous celled type. No glands were palpable.

Operation 1st October, 1948. A rectangular (Wookey) flap based on the left side of the neck was raised (as in Fig. VIII). The lower half of the sternomastoid muscle, and the left pre-tracheal muscles and anterior jugular vein were excised. The superior thyroid, middle thyroid and inferior thyroid vessels were ligated, the recurrent laryngeal nerve and the only parathyroid gland seen preserved, and the left lobe of the thyroid then removed. It was difficult to be sure of the limits of the tumour in the presence of post-radiation fibrosis and stenosis, but only a dense button of growth could be seen on the posterior aspect.

A 2½ inch cuff of oesophagus and pharynx was separated from the larynx and resected. The flap of skin was then folded in to the pre-vertebral region behind the trachea with two lines of subcutaneous chromic catgut, fixing it to the pre-vertebral muscles, and the divided oesophagus and pharynx sutured completely round to this skin, which was then folded S fashion back across the trachea. A tracheotomy tube was inserted as a temporary measure and the neck closed with the aid of a Thiersch graft on the right side.

Progress

The Thiersch graft took but there was little further evidence of healing. The suture lines did not heal well, and the tracheotomy opening slowly enlarged even after the tube was removed. The lower part of the flap sloughed. The patient had persistent vomiting which imperilled the airway. Feeding was at first down the oesophagus through the neck recess. On 13th October, 1948, a Senn gastrostomy was carried out, but vomiting and regurgitation continued. Death from bronchopneumonia occurred a month after the initial operation.

Comment

The success of this operation was doomed by the devitalized state of the tissues following irradiation, and large flap reconstructions should not be attempted under these circumstances. The gastrostomy should have been done pre operatively in view of subsequent events.

Pharyngo-Laryngectomy and Partial Oesophagectomy

Case 1

Mrs. E.G., aged 67, was seen on 30th June, 1948, complaining of increasing dysphagia over three months, and rapid loss of weight. Her blood pressure was 240/120 mm. of mercury. Biopsy confirmed the presence of a squamous celled carcinoma in the post-cricoid region (Fig. VII). No glands could be palpated.

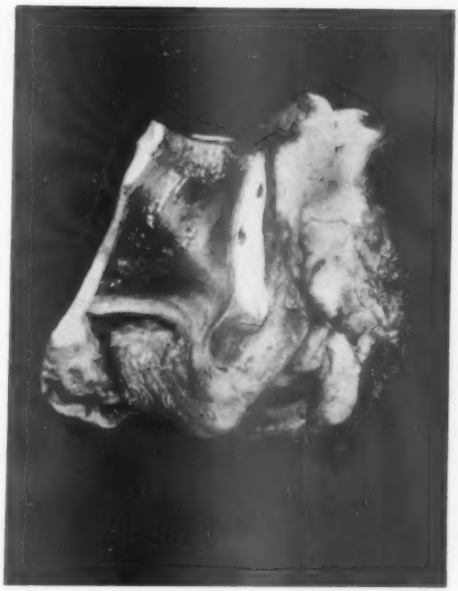

FIG. VII. Photograph of operative specimen—excised larynx, portion of pharynx and oesophagus, Case 2. Post-cricoid carcinoma.

At operation on 9th July, 1948, a Janeway gastrostomy was carried out. On 16th July, a left sided rectangular flap was raised (Fig. VIII) from across the neck, and the lower half of the left sternomastoid muscle, the left pre-tracheal muscles, and left lobe of the thyroid gland removed. Portion of the thyroid cartilage was removed and the pharynx opened above to define the tumour infiltration. The back of the larynx was seen to be extensively infiltrated, and its removal was determined.

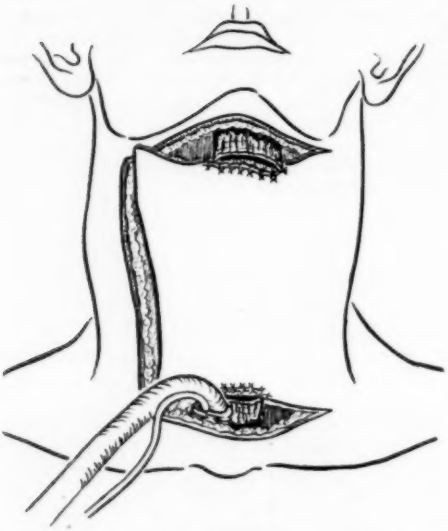

FIG. VIII. Diagram illustrating reconstruction by means of a large rectangular skin flap. Suture of the flap to the severed pharynx and oesophagus commenced.

The muscular attachments on the right side of the larynx were divided, and the superior laryngeal vessels and nerves divided and ligated on each side.

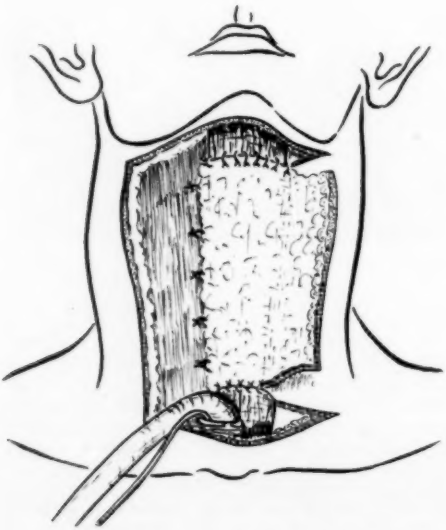

FIG. IX. Diagram showing further stage; the flap now folded back and suture continued.

The trachea was then divided well below the larynx, and a sterile cuffed tube inserted to replace the one *in situ* which was withdrawn. The oesophagus was divided an inch below palpable growth. The pharynx was then divided at the thyro-hyoid level, and the pharynx, larynx and cervical oesophagus dissected from the pre-vertebral tissues and the thyroid gland on the opposite side. One parathyroid gland on this side was left *in situ*. The other was resected along with an area of upper pole of thyroid gland, suspected of infiltration.

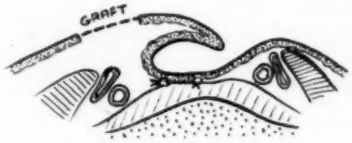

FIG. X. Diagram of neck, in section, showing arrangement of flap to form pharyngeal recess.

The first stage reconstruction was then carried out after the method of Wookey (1948) (illustrated by Figs. VIII, IX, X).

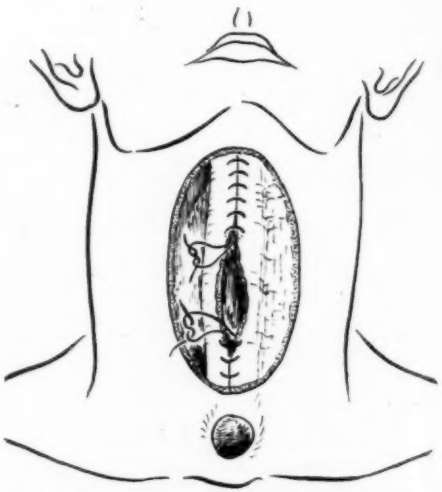

FIG. XI. Diagram of anterior aspect of neck showing the oval area of skin, raised about the pharyngeal and oesophageal stomata, being sewn as a tube.

The deep surface of the flap was fixed to the pre-vertebral tissues by two lines of interrupted chromic catgut, and the divided ends of oesophagus and pharynx sutured to the folded ends of the flap with fine interrupted silk. The remaining portion of the flap was folded back S-fashion across the midline. The open portion of the wound

was closed as far as possible by suture, and the deficient area on the right covered by a split skin graft. The trachea was brought through a separate opening and sutured to skin, and a large tracheotomy tube inserted. A Rehfuss tube was passed through the nose and guided through the deep skin recess into the oesophagus to "guide" passage of saliva.

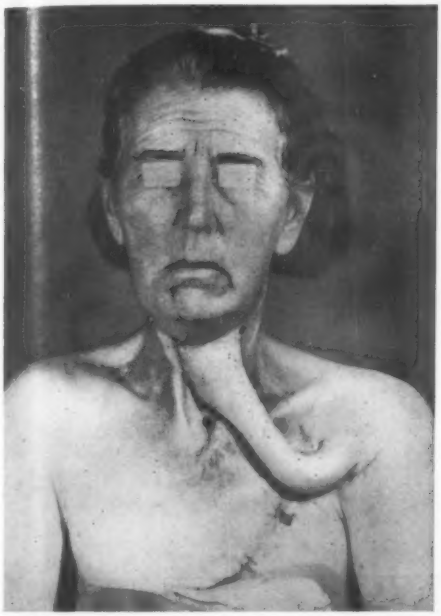

FIG. XII. Photograph of patient (Case 2) showing the final stages in reconstruction of skin pharynx. C.f. Fig. XIII.

Healing was excellent and there was no sloughing.

Subsequent operative steps were:—

11th August: Raising of left deltoideo-pectoral pedicle.

3rd September: Closure of skin oesophagus and migration of the pedicle graft to cover the bare area (Figs. XI, XII).

8th October: Detachment of pedicle (Fig. XIII).

29th October: Closure of the gastrostomy.

Progress

The patient swallowed a normal diet and radiated cheer. Less than three months after returning home she suddenly died of a coronary occlusion.

Comment

The growth appeared quite localized and the glands were not involved. Section exonerated the thyroid gland of involvement. Cure seemed within the grasp before her misfortune (Fig. VII).

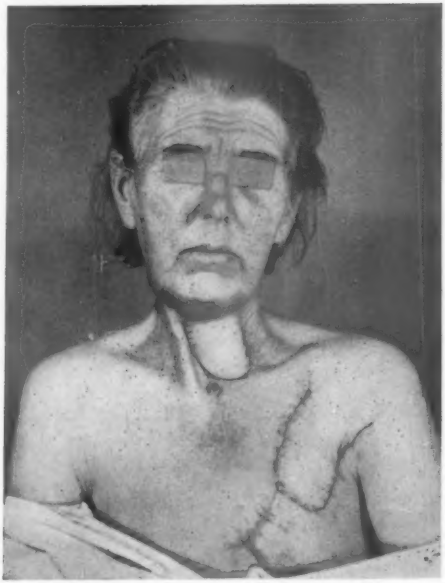

FIG. XIII. Photograph of patient (Case 2) showing reconstruction of pharynx. C.f. Fig. XII.

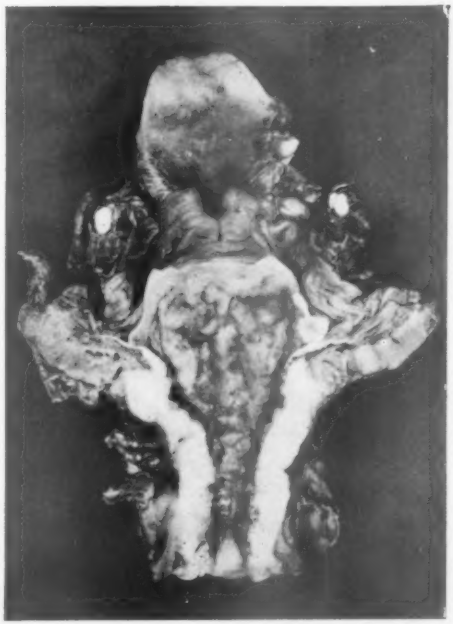

FIG. XIV. Photograph of specimen of excised pharynx, larynx and portion of oesophagus, Case 7. Extensive post-cricoid carcinoma.

Case 7

Miss O.P., aged 49, referred by Mr. John Shaw. Post-cricoid carcinoma with invasion of the larynx and early involvement of lymph nodes (Fig. XIV).

Gastrostomy was carried out on 8th January, 1950, and the same method of excision and primary reconstruction was employed. The subsequent secondary procedures were not so fortunate as in the previous case. Infection and sloughing of the flap occurred so that only the posterior wall was left. It became apparent that this shy spinster had lost all interest in life and she became wildly excited with minor procedures, such as penicillin injections, and was resentful of gastrostomy feeding. The oesophageal and tracheal openings lost their skin bridge and both stenosed.

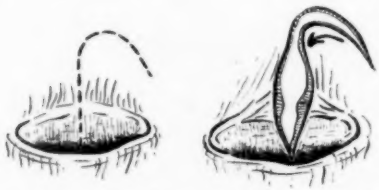

FIG. XV. Diagrams to show method of enlargement of a stenosed oesophageal opening, by rotation of a small V flap.

On 2nd March, 1950, a small skin flap was raised from the chest and sewn between these two openings. A split skin graft covered the deficiency. At the same time a pedicle flap was raised. Subsequent hysterical violence partly dislodged the former flap.

On 27th March, the pedicle graft was "delayed."

On 13th April, the oesophageal opening was enlarged by a V plastic (Fig. XV), and the major closure of the pharyngostome effected. The pedicle was migrated. (This pedicle graft did not take well to the fibrous tissue and for a time the new pharynx gaped widely open. Slowly it closed.)

On 26th July, the pedicle was detached (Fig. XVI).

On 4th August, — closure of the gastrostomy.

Subsequent Progress

She became very well and gained 3 stone in weight. There has been no evidence of recurrence more than two years after excision. She is working actively in a factory. The loss of speech seems to suit her shy personality and, though the speech therapist reported progress in pharyngeal speech, she will make no further attempt to talk. She appears to be quite happy now.

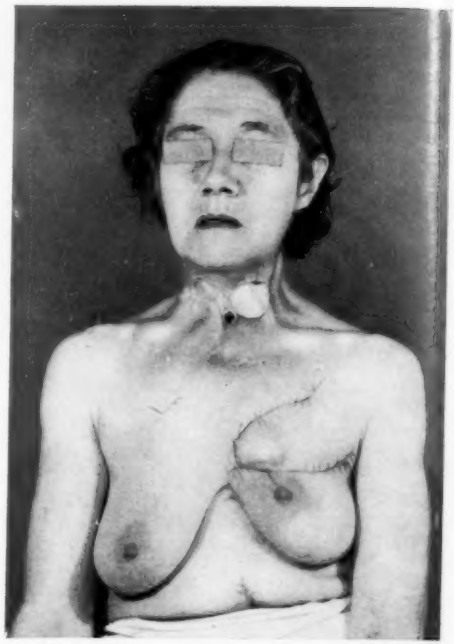

FIG. XVI. Photograph of the patient in whom a reconstruction has been completed, Case 7.

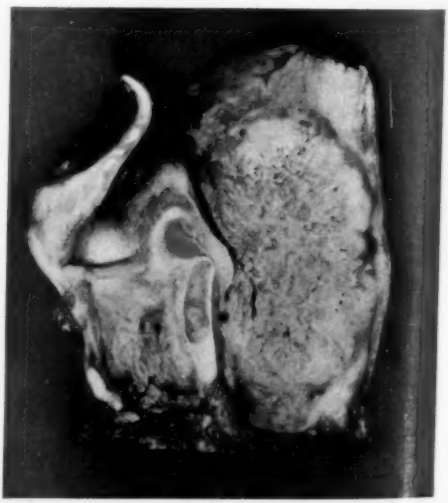

FIG. XVII. Photograph of the specimen removed from Case 7. showing the massive carcinoma in post-cricoid region. The lumen of the laryngo-pharynx is reduced to a narrow slit.

Case 5

Mrs. M.B., aged 56. She suffered from a huge post-cricoid growth with bilateral lymph node deposits (Fig. XVIII). Her dysphagia was nearly complete and she was scarcely able to breath. Her general condition was most wretched.

The sequence of treatment was as follows:—

20th August, 1949: Oesophagoscopy and biopsy. Janeway gastrostomy.

8th September: Pharyngo-laryngectomy and partial oesophagectomy, radical dissection of glands on the neck on the right side, but sparing the jugular vein.

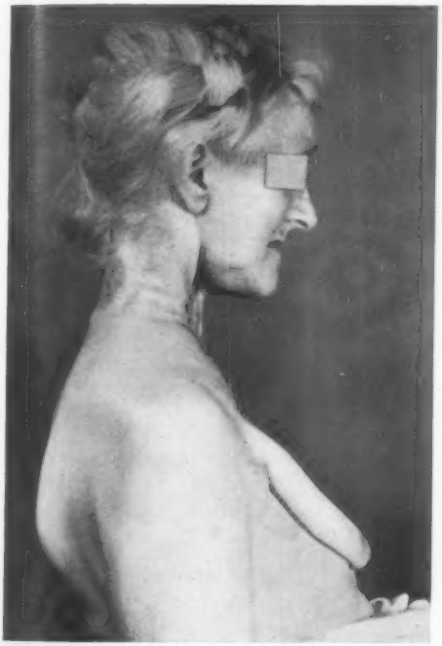

FIG. XVIII. Photograph of patient following pharyngo-laryngectomy; pedicle raised. Reconstruction was never completed due to secondary deposits which are seen as a swelling at the base of the neck.

It was necessary to remove the pharynx to almost the level of the uvula.

The flap sloughed in part as would be expected.

13th October: Radical dissection of glands of the neck on the left side, including the jugular vein.

15th November: Closure of the pharyngostome. A split skin graft anteriorly.

FIG. XIX. X-ray appearances on barium swallow, Case 14, of a massive carcinoma which extended from above the larynx to below the clavicle.

Progress

Further lymph node deposits were growing up from the mediastinum by the time of completion.

The patient swallowed naturally for only a short time and the gastrostomy was retained.

Her morale remained splendid until her final deterioration and death from bronchopneumonia on 10th March, 1950. There were extensive lymph node metastases and lung deposits.

Comment

Skin reconstruction is unlikely to succeed in advanced cases with lymphatic metastases. Lymph node dissection interferes with the blood supply of the flap and a large rectangular flap was unwise.

Experience with two further advanced cases confirmed the view that operations with skin plastic reconstruction should not be undertaken in the presence of heavy gland deposits (Fig. XVIII).

POLYTHENE TUBE AND SKIN GRAFT

Case 14.

Mrs. C.B.G., aged 55. An extremely advanced carcinoma extended from the level of the epiglottis to the thoracic oesophagus. The larynx and trachea

were heavily invaded, and the growth was shown subsequently to invade the pre-vertebral muscles and the thyroid gland. There were heavy lymphatic metastases in the left side of the neck.

It appeared that she had suffered from a long-standing hypopharyngitis and "small swallow" and that for seven months she had experienced sore throat and increasing dysphagia. Her tonsils were erroneously removed.

She then saw Mr. C. Gardiner who at once recognized the condition and referred her on 28th February, 1952.

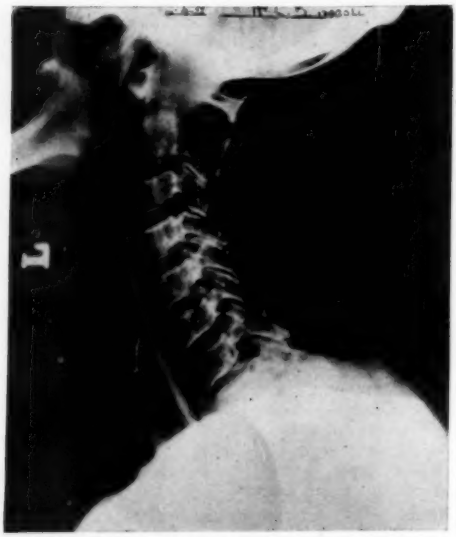

FIG. XX. X-ray appearance of grafted polythene tube *in situ* (Case 14). It extended to the level of the aortic arch. Excellent swallowing without leakage.

Intubation proved fruitless owing to the length of the growth and a gastrostomy was carried out on 4th March. She developed progressive respiratory obstruction.

On 17th March, under general anaesthesia, the extensive lateral pharyngotomy incision (Fig. I) was made. An extensive radical dissection of the glands of the left side of the neck including the sternomastoid and jugular vein was effected. The larynx and pharynx were freely exposed following removal of the left infra-hyoid muscles and the left lobe of the thyroid.

The larynx, pharynx and oesophagus were removed in a block from the back of the tongue down to the thoracic cavity. Due to the infiltration of the thyroid only one parathyroid gland was located and left in position on the left side. Some malignancy was left on the pre-vertebral tissues.

Mr. J. Devine assisted in the shaping of a polythene tubular mould 7 inches in length, with a general internal diameter of ½ inch, and funnel-shaped upper expansion. This was covered with a split skin graft sutured in position. This was inserted in the open pharynx and lightly sutured by chromic catgut passing through drill holes in the upper rim. The lower end fitted snugly in the thoracic oesophagus without suture.

The remnants of the thyroid gland and infra-hyoid muscles were wrapped about the tube and graft as far as possible and the neck then closed by skin suture. Two small drain tubes were inserted.

The trachea was sutured to skin through a separate opening.

Progress

Pre- and post-operative X-rays are reproduced (Figs. XIX, XX). There was no leakage from the tube pharynx and practically no infection. The patient swallowed with fair comfort and no leakage after the 7th post-operative day.

At this stage she had tetanic spasms which required parenteral calcium. This has now subsided. She now breathes quite comfortably. No further injections of calcium are necessary though she takes oral calcium preparations.

Comment

Recurrence seems certain, but if she continues to tolerate the polythene tubing, the grafted track should remain open. Under the circumstances it seems unwise to remove it as would otherwise be done. If the method has even a measure of success in such an extreme case, there seems to be bright prospects of avoiding time-consuming skin plastic procedures in less intractable cases.

POST-OPERATIVE TREATMENT

These patients require expert nursing and close personal supervision of dressings. Usually little resuscitation is required post-operatively, but an essential requirement is effective suction to clear the trachea and bronchi in the early post-operative days. A soft catheter should be passed at frequent intervals through the tracheotomy tube well into the trachea and bronchi if necessary. With this precaution serious respiratory complications are rare.

Suction is also useful to dispose of saliva from open pharyngostomes during reconstruction. After pharyngeal reconstruction

food is not usually given by mouth for a week and nutrition is maintained by nasal tube or gastrostomy.

DISCUSSION OF OPERATIVE METHODS

Palliative and Minor Procedures

1. *Gastrostomy.* Gross dysphagia may necessitate gastrostomy. Unless, however, the growth is subsequently removed, the patient suffers great misery from regurgitation of foul saliva and secretions, which also irritate the air passages. If respiratory obstruction dictates tracheotomy in addition life is barely tolerable and unlikely to be greatly prolonged. Where a gastrostomy is likely to be permanent or prolonged, a tube-flap gastrostomy of the Janeway type is to be preferred. Where it is a temporary expedient in pharyngeal reconstruction the Senn type of gastrostomy has the advantage that it may close rapidly when the tube is removed without operative closure. A wide range of foods may be administered per medium of a "grease gun."

2. *Tracheotomy.* This procedure will extend life slightly but does not afford much comfort to the patient whose larynx is blocked by tumour tissue. The viscid secretions obstruct the tube and cause great distress. The patient has little if any voice.

If, however, it is possible to excise the larynx even as a palliative procedure relief of respiratory distress is attained by a large tracheal stoma well removed from the cancer site.

It may be necessary to perform a tracheotomy as a preliminary measure to relieve urgent respiratory distress and bring the patient into suitable condition for operation.

When this is the case it is fortunate if it is performed by the surgeon who undertakes the subsequent treament, in that care should be taken to plan the tracheotomy incision so that it may be included in the incision for the next stage, and not form a defect in a flap of skin required for reconstruction. A low transverse incision often meets this requirement.

3. *Intubation* — for example, Souttar's tube or polythene tubing.

Polythene tubing is more soft and flexible, and can be moulded at a suitable temperature and adjusted readily to any length.

Even Souttar's tubes may be surprisingly well tolerated in the immediate post-cricoid region if inserted into malignant tissue.

For several reasons the relief of dysphagia may be very incomplete.

MAJOR OPERATIVE PROCEDURES

In a suitable case a tumour of the pharynx or cervical oesophagus may be removed with adequate margin, leaving the larynx undisturbed. It is usually necessary to reconstruct the pharynx by some plastic procedure.

1. Median Pharyngotomy

This does not provide a satisfactory exposure to most growths in the region and does not lend itself to lymph node dissection.

2. Lateral Pharyngotomy with Conservation of Most of the Larynx

This was used extensively by Trotter who secured wide exposure of the pharynx by excising part of the thyroid cartilage, the hyoid bone and, if necessary, dividing the mandible. It provides ready exposure for a block dissection of lymph nodes.

There appears to be no necessity to retain the sternomastoid on the affected side in order that this structure may be stitched to pre-vertebral tissues to "shut off the mediastinum."

In the personal experience of the writer, who has seen mainly less tractable malignancies of the region, this approach is inadequate for most post-cricoid neoplasms since these usually invade the larynx, and are best dealt with by pharyngo-laryngectomy, with provision of skin flaps for reconstruction employing skin from both sides of the neck.

It is also likely to provide an inadequate margin of excision of growths of the upper laryngo-pharynx in most cases, unless the

larynx is excised. It is, however, readily modified to an excellent approach with which to carry out a laryngectomy extended to deal with the involved side of the pharynx, and a block dissection of cervical nodes on the affected side.

It has been found possible in many such cases to do a primary pharyngeal reconstruction with mucosa from the other side of the expanded cone of the pharynx which only becomes available with removal of the larynx. The type of incision recommended is illustrated (Figs. I and II). Should the extent of the malignancy prove such at operation that it is necessary to excise a complete segment of pharynx and cervical oesophagus as in the usual pharyngo-laryngectomy, there is a sufficiently large skin flap to provide a posterior wall and small ridge for partial reconstruction of the pharynx.

At the same time this flap is not so large that sloughing will necessarily follow block dissection of the lymph nodes, and consequent impairment of blood supply, as in the use of the large transverse flap (Fig. VIII).

It is considered advisable to have the tracheal opening well removed from the major line of incision, where a small circle of skin may be excised.

3. Pharyngo-Laryngectomy

The excision of a complete block of pharynx, oesophagus and larynx offers the best hope of cure in any post-cricoid carcinoma, and in the case of extensive malignancy arising in the upper laryngo-pharynx.

It may be applicable to certain late and widely invasive intrinsic cancers of the larynx. The paradox of this method of radical excision is that consideration of the viability of skin flaps for reconstruction has led to some conservatism in the dissection of lymph nodes. Most observers are pessimistic as to the possibility of dealing successfully with post-cricoid carcinomata in which there is clinical evidence of lymph node involvement.

In such a case the writer has carried out pharyngo-laryngectomy combined with block dissection on one side, then a later lymph node dissection on the opposite side, prior to embarking on closure of the pharyngostome. Mediastinal deposits still defeated ultimate success.

Large rectangular transverse flaps form a ready basis of first stage reconstruction of the pharynx, and when used successfully render the subsequent closure very easy. They should not be employed where lymph node dissection is necessary, or where the growth is very extensive, for not only will blood supply suffer in the dissection, but some tension is likely to arise in bridging the gap.

In such cases two smaller lateral flaps on either side of a vertical incision seems preferable, though this vertical incision may be placed asymmetrically to avoid a line of suture above the tracheal stoma.

It is considered most desirable to make the tracheal stoma through a separate circle of excised skin below the main incision to ensure a viable skin bridge between the oesophageal and tracheal openings. Failure to do this may necessitate plastic procedures to separate these structures.

Difficulties may arise with extensive downward extension in the trachea, particularly as this occurs commonly on the posterior wall which is most difficult to get up to the skin. This may be dealt with by rotating a large skin flap off the chest wall and sewing it round the severed trachea before this is permitted to retreat into the chest with its funnel of attached skin. The denuded area on the chest wall is then covered with a split skin graft.

Subsequent Stages in Pharyngeal Reconstruction

Where large transverse skin flaps are used to form a recess in the initial excision operation, at least five weeks must elapse before closure is attempted.

An oval skin incision is made to incorporate the pharyngeal and oesophageal openings (Figs. XI, XXI) and peripheral skin is then mobilized and sewn into a tube with the knots tied on the inner side. A skin

graft must then be applied to the bare area over this buried tube. Thiersch grafts have been employed, Wookey (1948), but the writer has found a deltoideo-pectoral pedicle on the same side preferable in most cases (Fig. XII).

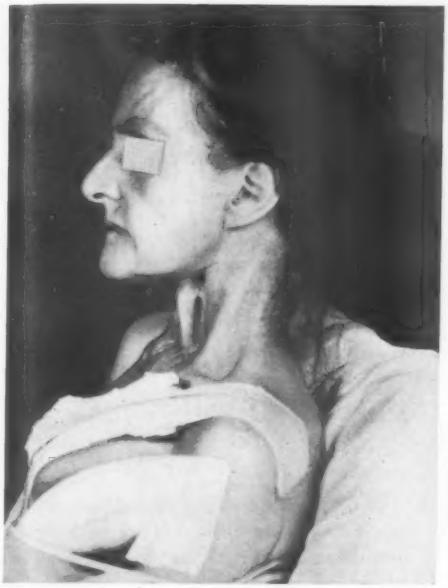

FIG. XXI. Photograph of a patient following a pharyngeal recess shallow in this case due to loss of some skin by sloughing.

This should, therefore, be raised two to three weeks after the excision of the growth to avoid time loss.

During the period between the first stage of reconstruction and subsequent closure, varying degress of stenosis of the oesophageal opening may arise. The opening should be made as large as possible initially by oblique section of the gullet and careful suture to the skin. Subsequent dilatation prior to closure will assist.

It is, however, a mistake to effect closure with this opening still narrow, under the belief that subsequent dilatation can be done via the patient's mouth.

The simple V plastic shown in Fig. XV is most effective and the writer has found it quite feasible to do this at the same time as the skin tube is closed. Once the patient is swallowing well, there is little fear of further contracture.

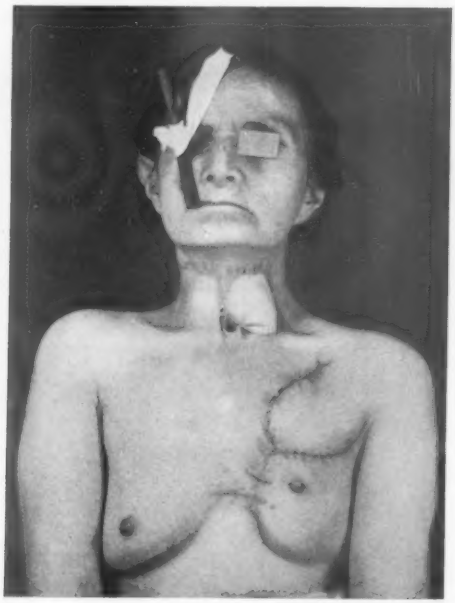

FIG. XXII. Photograph of same patient as shown in Fig. XXI when pharynx reconstructed.

The beard area may present difficulty in males in that if skin from this area is turned in, the growth of hair may block the passage of food through the skin pharynx. In one male case of the writer's, patient work was carried out to epilate the required portion of skin employing a diathermy needle. Nevertheless, a few hairs grew up to form a tangle in the food passage and caused a little intermittent trouble. Migrated grafted skin could, no doubt, be used for the entire inner tube but this would be likely to consume much time.

Primary Closure Over a Polythene Tube and Split Skin Graft

This method has obvious advantages if the pharyngeal function proves satisfactory after removal of the tube, and operations of this type may replace staged procedures (Fig. XXII). The method has been introduced

very recently and it is not yet proven. At the present time it would seem to offer the best hope of palliation for advanced growths, particularly where metastases are present.

It has obvious attractions in the case of males with bearded necks.

OPERATIVE RESULTS — MAJOR PROCEDURES

These have been much better with lesions of the upper laryngo-pharynx (epilaryngeal) than those of the lower laryngo-pharynx and cervical oesophagus.

There has been only one late operative death in the numerous operations associated with 20 major excisions and associated reconstructions.

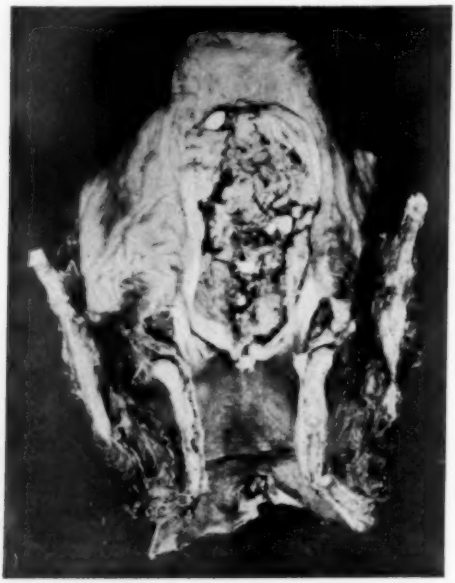

FIG. XXIII. Photograph of an operative specimen showing extensive carcinoma extending from the posterior surface of the epiglottis.

There is insufficient passage of time to assess late results as yet. The longest survivor in good health and free of recurrence has survived two years and nine months.

Of the whole group, 5 patients have as yet survived more than two years and of these, 4 are in good health without recurrence.

Epilaryngeal Group — 9 patients.

6 are surviving in good health. One of these has a recurrence which is well controlled by deep X-ray therapy eighteen months after operation.

2 died — metastases approximately twelve months.

1 died — coronary occlusion three months.

Post-cricoid and Oesophageal—10 patients.

2 survive in good health over two years.

3 others surviving eighteen months, six months, six weeks respectively.

1 died five months after operation from coronary disease, with no recurrence.

1 died, two years, two months—recurrence.

2 died six months after operation—recurrence.

1 died, one month after operation.

SUMMARY

1. The difficulties of treatment of carcinomata of the laryngo-pharynx and cervical oesophagus are outlined, and some account given of historical developments.

2. Reference is made to some misconceptions about treatment and the place of radiotherapy and surgery.

3. Brief reference is made to pathology, symptomatology and diagnosis.

4. Operative treatment is illustrated by methods employed in a personal series of 25 cases, averaging 62 years. 20 major excision operations were carried out, and numerous secondary precedures mainly associated with reconstruction of an artificial pharynx. There was one late post-operative death.

5. Operative methods are discussed, and some account is given of operative results.

ACKNOWLEDGEMENT

My thanks are due to Dr. P. A. Crooke for drawings used in illustrations.

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CHOLECYSTITIS GLANDULARIS

(Rokitansky-Luschka-Aschoff Sinuses)

AND RELATED CONDITIONS

By E. S. J. King

Department of Pathology, University of Melbourne

Antipholus of Syracuse:
And I was ta'en for him, and he for me,
And thereupon these errors are arose.
The Comedy of Errors:
Act. V, Sc. I, l. 390.

CHOLECYSTITIS glandularis is a condition in which there is a downgrowth of sinuses from the surface epithelium into the layers of the wall of the gall-bladder and these may be so large as to give the appearance of out-pouchings of the lumen or diverticula. The condition occurs in various macroscopic forms which, however, are fundamentally similar in their structure. The sinuses (and where these are dilated, the pouches or cysts) are lined by an epithelium which is like that of the mucosa of the gall-bladder or of one of the forms of intestinal epithelium.

This condition is commonly seen and is well recognized, but since knowledge of it has passed through various vicissitudes which still influence to some degree opinions regarding it, it is desirable to discuss the matter here again. There are other conditions which may in some measure resemble this one histologically and, since the different kinds of glands in the gall-bladder wall have different origins, their separation is important.

There are three distinct and different conditions which will be considered individually.

1. Cholecystitis glandularis proliferans—sometimes referred to as Rokitansky-Aschoff sinuses and, at other times, Luschka sinuses or glands.

2. Hyperplasia of the biliary ducts—sometimes known as the "true Luschka ducts."

3. Mesothelial glands which have grown from the peritoneum.

Much of the confusion which has occurred regarding these conditions arises from an eponymous terminology so that it is necessary to consider this aspect of the subject somewhat fully.

Historical Review

Pouches in the wall of the gall-bladder communicating with the lumen were first described in 1842 by von Rokitansky. In 1858, these glands or pouches were observed also by Luschka and his method of demonstrating them is of some significance. The mucous membrane was dissected from the wall and treated with acetic acid (and thus made transparent) and then examined on a glass plate by transmitted light; he was thus able to count the number of glands. It is apparent that the structures described here by Luschka are the same as those described by von Rokitansky. In 1905 Aschoff gave a more complete description than had been provided previously of these structures and referred to the glands and crypts in the wall as Luschka's glands.

Luschka, however, in 1863, had described other glands which he referred to as aberrant bile ducts. These occurred only in the perimuscular coat and did not communicate with the lumen and indeed Luschka could not show that they communicated with bile ducts. However, they were morphologically very similar to bile ducts. Luschka observed these glands both on the hepatic aspect of the gall-bladder and in the sub-peritoneal coat.

Aschoff (1905), observing both the crypts communicating with the lumen and sub-peritoneal glands, considered that the last actually were in continuity with the former glands, but that this was difficult to demonstrate owing to tortuosity. He recognized that there were some glands of biliary duct structure but stated that they occurred only on the surface of the gall-bladder in contact with the liver. Consequently Aschoff considered that Luschka had been wrong in interpreting the sub-peritoneal ducts as aberrant bile ducts and he regarded them as being the deeper out-pouchings of the gall-bladder mucosa.

Within a short time it was emphasized by Shikinami (1908) and Jurisch (1909) that the structures described by Aschoff were different from the ducts that had been described by Luschka. Neither of these writers appears to have appreciated the significance of Luschka's second observation and Shikinami designated the sub-peritoneal ducts as "Aschoff's ducts."

In 1927 Halpert made a valuable contribution to the subject in which he reviewed the previous literature and as the result of an examination of a series of gall-bladders, both foetal and adult, he emphasized the difference between the two kinds of structures. He distinguished clearly between the sinuses communicating with the lumen of the gall-bladder — the "Rokitansky-Aschoff sinuses" and the peripherally situated ducts —the "true Luschka ducts." This attempt to clarify the situation has not been as successful as might have been hoped, probably because many readers retain the mental impression of Luschka's simple experiment to demonstrate the sinuses in the gall-bladder wall. If it be desirable to retain an eponymous terminology at all it might be wise to refer to the Luschka (or Rokitansky-Aschoff) sinuses and the Luschka ducts.

Relatively little attention seems to have been paid to these structures until, in 1922, Bodnár described the gross distension of some of the sinuses of crypts with formation of cysts—a condition to which he gave the name cholecystitis cystica. In 1923, Nicholson described the metaplasia which occurs in the epithelium in the walls of chronically inflamed gall-bladders. In 1931, King and MacCallum described the various localized and diffuse thickenings that occur in the wall of the gall-bladder associated with the development of these glands. The relation of these conditions to the less conspicuous examples where only occasional sinuses are present was appreciated and, in an attempt to supply a pathological rather than an eponymous terminology, the name cholecystitis glandularis proliferans was suggested for the condition.

It should be emphasized that this term cholecystitis glandularis applies to the same condition as has been designated Rokitansky-Aschoff or Luschka sinuses. It differs only in that it comprehends a somewhat larger group since cases, in which easily demonstrated sinuses are not present, are also included. The term also emphasizes the development of the condition in post-natal life (associated with inflammatory changes), and that it is found, therefore, almost solely in adults. A cause for confusion is that the "aberrant bile ducts" or "true Luschka ducts" may be found in young children and, when they are not distinguished clearly from the sinuses, these are therefore thought to be of developmental origin.

That the sinuses should be demonstrated on X-ray examination during cholecystography was to be expected and this was described and illustrated in 1948 by March.

MORPHOLOGICAL APPEARANCES

Although glands occurring in the gall-bladder wall are of three quite distinct types, only those which develop by downgrowth from the mucosa of the organ present characteristic gross appearances. The other two types mentioned above, however, show characteristic histological forms. All of these may occur together in the one organ, but they are distinguished much more easily and with greater certainty when they occur separately; indeed, it is in such circumstances that their special characteristics are determined with certainty and enable them to be segregated when they occur together. They will therefore be considered here in turn.

Cholecystitis Glandularis Proliferans

As indicated previously, this condition is one in which there is a downgrowth of the epithelium into the subjacent tissues with the formation of sinuses and out-pouchings (Fig. VIIIA). It is doubtful whether this

phenomenon occurs at any time apart from inflammatory (using the term in a broad sense) conditions; indeed, it has long been recognized that probably they are not to be found in the normal gall-bladder and their presence is an indication of previous damage.

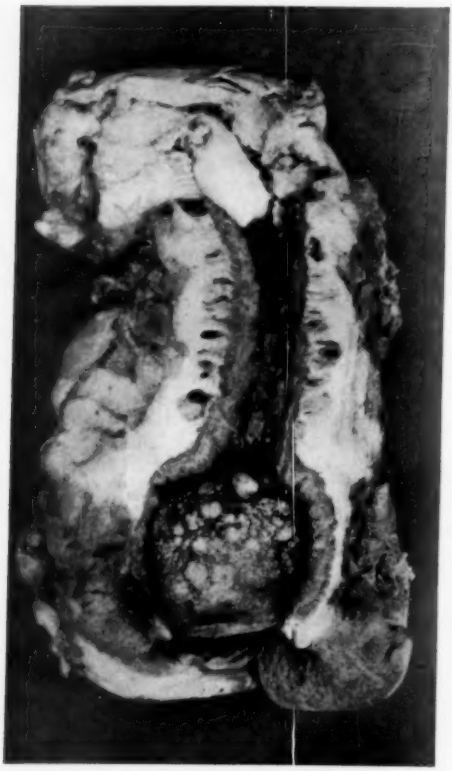

FIG. I. Photograph of a specimen of the gall-bladder from a male aged 55 years, removed at operation. There is a large, single cholesterol calculus in the cavity, and numerous dilated crypts in the wall, communicating with the lumen, are to be seen.

Macroscopic Appearances

The gross features of the condition differ considerably, covering a range from relatively normal-appearing organs, in which the crypts can be found by special examination, to those in which there is gross and easily demonstrable thickening of the wall of either localized or diffuse character. There is also considerable variation according to whether the gall-bladder is inflamed or not.

Sinuses and Cysts without Cholecystitis

The mildest degree is that in which there are (a) only a few pouches scattered over the wall or (b) some proliferation of the mucosa without significant invasion of the wall. (a) The first, even when not prominent, can often be recognized macroscopically. The original descriptions by Luschka were of such pouches and were observed by dissecting the mucous membrane from the wall; when this was held up to the light the small pouches could be recognized. These are sometimes seen in relatively normal-appearing gall-bladders but it is usual to find some thickening of the wall. For this reason it is considered that the pouches are not, in the vast majority of cases, a normal phenomenon but are associated with some degree of old inflammatory changes in the wall. (b) In some cases there is a thickening of the mucous layer but often a degree of change which is histologically striking may not be recognizable macroscopically.

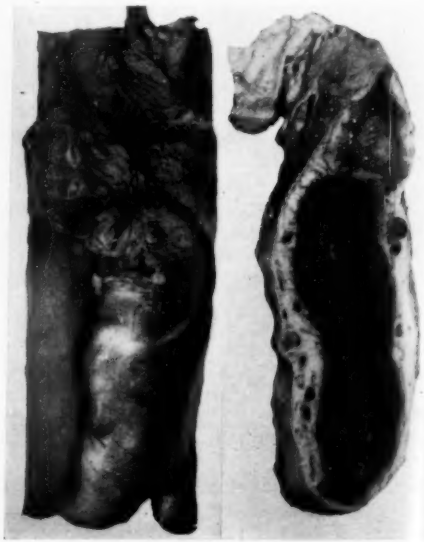

FIG. II. Photographs of the gall-bladder, viewed from the external aspect and also in section, from a male aged 54 years (incidental observation at post-mortem—death due to cardiovascular syphilis). The thickenings in the wall of the gall-bladder as seen from the external surface are shown in one, and the calculi in crypts in various parts of the wall in the other, photograph.

In other cases there are localized or diffuse areas of thickening (King and MacCallum, 1931) and when these are examined carefully it is found that there are numerous small crypts and spaces through the wall. They may be localized largely to the superficial areas (Fig. I) but sometimes extend deeply down to the peritoneum. Indeed, they may be most prominent on the peritoneal aspect (Fig. II).

Some of these areas have been described as tumours of various kinds. The problem here is the same as elsewhere, that is to say, it is one of distinguishing between a slow neoplastic process and a hyperplasia. The distinguishing feature, of course, is the inevitable progressive nature of the neoplasm and it would seem quite clear that the majority of these cases cannot possibly fall into that group.

In some cases the crypts and glands are distended to form cysts and these cysts may contain calculi (Fig. II).

Sinuses and Crypts with Acute Cholecystitis

In these cases the gall-bladder wall is usually grossly thickened and the crypts and sinuses may be seen scattered through the wall. A characteristic form is one in which there are numerous demonstrable and sometimes dilated cysts in the swollen submucous region (Fig. I). In other examples there are dilated glands either in the muscular coat or in the sub-peritoneal coat (Fig. III).

Histological Appearances

The projections of the mucosa into the subjacent tissues may be few in number or may be very numerous, in the second case sometimes giving the appearance of gastric mucosa or intestinal villi and glands. In such cases their communication with the lumen of the organ is without question.

The sinuses and glands may be confined to the immediate submucous region or they may extend down into the muscle and even through the muscle into the sub-peritoneal coat. Although occasionally the communication of the deeper glands with the lumen is demonstrable easily, in many cases, owing to their oblique (in relation to the plane of the section) or tortuous course, such may be demonstrable only by serial sections.

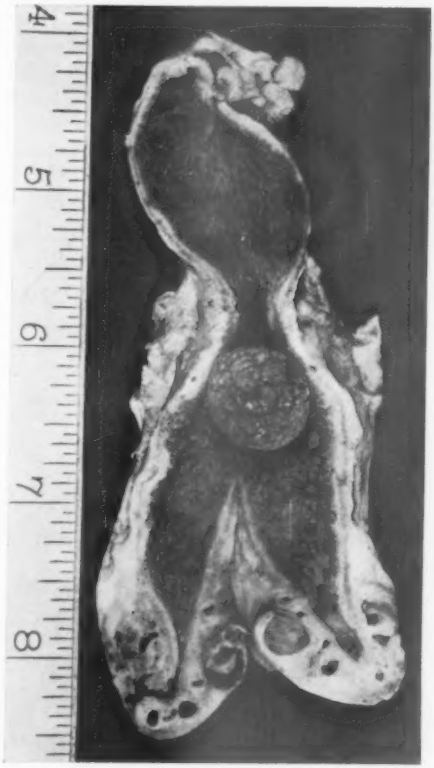

FIG. III. Photograph of the gall-bladder from a female aged 57 years removed at operation showing a cholesterol calculus in the gall-bladder and numerous calculi in crypts in the wall.

The crypts and pouches are lined often by typical gall-bladder epithelium but there may be a change; either an intestinal type of epithelium or even occasionally stratified or squamous epithelium is formed. Underneath this layer there are frequently other types of epithelium, commonly in the form of gastro-duodenal glands, sometimes mucous glands (King, 1930) and less commonly pancreatic glands.

The development of these glands is a very good example of metaplasia and one which is commonly quoted. It is the presence of

these glands in so many of these cases that demands a terminology other than an eponymous one and indeed it was the observation of these glands that suggested the term cholecystitis glandularis. The term Rokitansky-Aschoff sinus would suggest that the epithelium of the gall-bladder cavity has protruded out into the muscle of the organ but that this is all that has happened. Indeed this was all that the original observers described. At the same time there is no real distinction between the two conditions and it would be most undesirable and artificial to distinguish two types, as, for example, by applying the term of Aschoff sinuses to those in which there was not any metaplasia and some other term to those in which there was such.

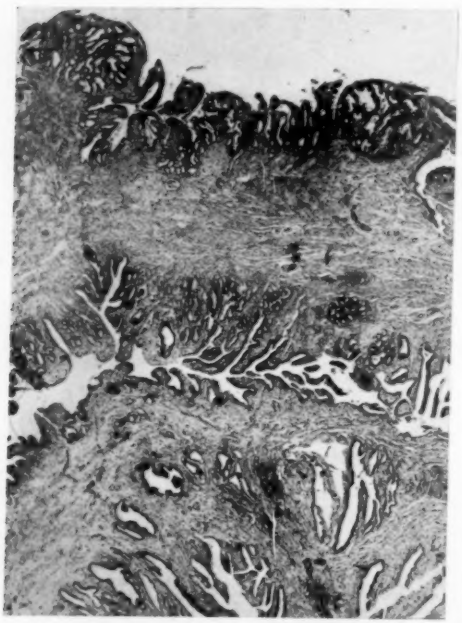

FIG. IV. Photomicrograph of a section of a gall-bladder showing a typical example of multiple crypts in the wall—cholecystitis glandularis. (x 12)

In the cases of infection of the gall-bladder numerous wandering cells, polymorphonuclear leucocytes and macrophages, are seen throughout the wall and there may be gross oedema. The essential features of the condition, however, differ in no way, in these circumstances, from those in which there is no significant active inflammation.

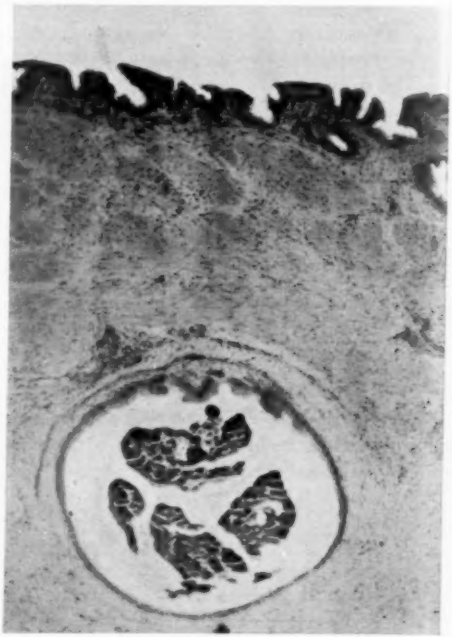

FIG. V. Photomicrograph of a section of portion of the wall of a gall-bladder in which there were intra-mural calculi. Here is a gland in the muscle coat containing biliary material. (x 70)

Formation of Cysts or Diverticula

Cysts, sometimes of considerable size, may be found in any of the layers of the gall-bladder. These do not present any special aetiological features but are due to distension of some or other of the glands or crypts. The communication of these with the lumen —and there is always a confluence—is by a narrow canal and it may be difficult, without serial section, to determine that there is such a connection; but careful search will show this. In some cases the opening into the cavity of the gall-bladder is a wide one and the cavity then is merely a pouching from the lumen of the organ. It is these wide necked spaces which are quite properly designated diverticula.

The cysts may be seen sometimes scattered along the submucous area in a regular line. At other times either occasional ones or groups constituting a congery of cysts will be seen in the muscle layer. When cysts are present on the sub-peritoneal surface they may be easily recognized particularly when containing calculi, in the intact organ (Fig. II).

FIG. VI. Photomicrograph of portion of the wall of a gall-bladder (shown in Fig. II) in which there were intra-mural calculi. In this case the space containing the biliary material which is lined, at least partly, by epithelium is seen to be in communication with the main lumen. (x 15)

Formation of Calculi in Cysts

Calculi in the wall of the gall-bladder were observed and described by Rokitansky but relatively little attention seems to have been paid to them since then. These "calculi" vary greatly in size and in consistence. They may be merely masses of pigmented mud or they may be as well organized as any of the calculi seen in the lumen of the gall-bladder. The calculi are of the same kind as those seen in the gall-bladder, that is to say, they may be cholesterol stones or pigment stones but are usually of the mixed type. In histological sections they are recognized as being composed of material which is pigmented and contains numerous crystals often of the cholesterol type (Fig. V).

In many of these cases the communication of the cyst with the lumen is very small and may be difficult to find, but such can be demonstrated by serial section, or occasionally, a lucky section (Fig. VI) demonstrates the cyst to be a crypt in communication with the lumen.

The calculi, when they are in a superficial (submucous) cyst, may partly project into the lumen of the gall-bladder (Fig. VII). At other times they are found in the muscle coat and they may be seen in cysts in the sub-peritoneal coat in which case they are recognized as firm or hard nodules projecting from the peritoneal surface of the gall-bladder (Figs. II and III).

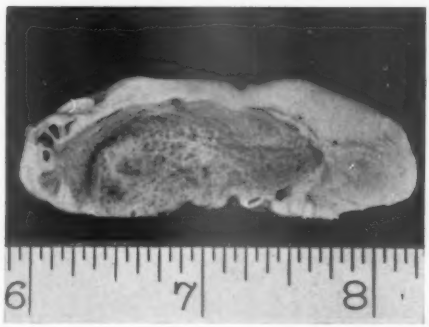

FIG. VII. Photograph of a gall-bladder from a male aged 50 years showing small calculi in the wall. These are to be seen where the wall has been cut but in addition they may be observed projecting towards the lumen through the openings of the crypts in the mucosa.

Usually, though not always, calculi of a similar kind are to be found in the lumen of the gall-bladder. This would suggest that the mode of formation of the calculi in cysts and the factors determining this are the same as for the calculi in the main cavity of the gall-bladder, except that in so far as stasis is more likely to occur in a cyst than in the cavity of the gall-bladder so calculi occur more readily in them. This is supported by the observation of the actual more frequent occurrence of calculi in these crypts (when they are present) than in the cavity of the gall-bladder itself.

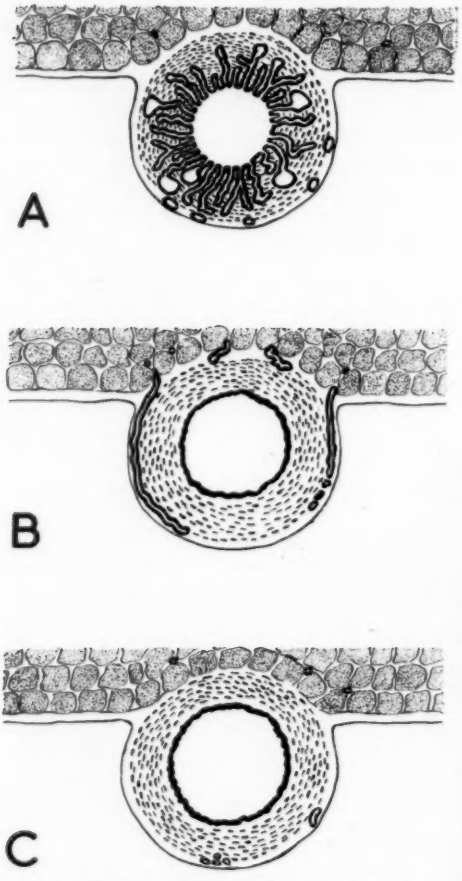

FIG. VIII. Drawings showing diagrammatically the relation of the three kinds of sub-peritoneal glands to each other.

(a) There is invasion of the wall by downgrowths of epithelial glands forming sinuses and cysts. Some of these may extend to the sub-peritoneal layer and, because of tortuosity, their communication with the remaining sinuses may not be apparent in any one section.

(b) Sub-peritoneal biliary ducts may extend round from the hepatic region for a considerable distance. Occasionally a long length of duct may be seen in one section, but in other cases serial sections may be necessary to demonstrate the relation of parts distant from the liver to the hepatic ducts.

(c) Small sub-peritoneal glands in the absence of either of the other types may suggest a peritoneal origin. The histological appearance (Fig. XII) will confirm the suggestion.

Hyperplasia of Biliary Ducts (Luschka's Ducts)

The aberrant ducts are found less commonly than the sinuses just described but occur characteristically in the peripheral, that is the sub-peritoneal layer of the gall-bladder wall (Fig. VIIIB). They thus present quite a different picture from the sinuses in the gall-bladder wall; this difference is shown diagrammatically in Fig. VIII. The ducts, in contra-distinction to the sinuses, never communicate with the lumen.

They are to be found most often on the hepatic aspect of the gall-bladder (Fig. IX) and often along the margin of the *fossa vesicae felleae*. Occasionally they are to be found under the peritoneal coat at a distance from the liver and occasionally a fortunate section may show the duct passing round for some considerable distance.

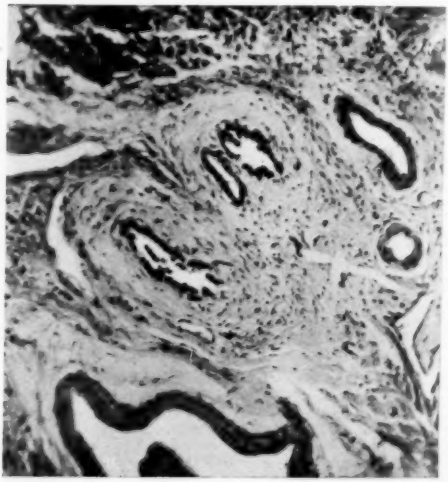

FIG. IX. Photomicrograph of portion of the wall of a gall-bladder from a male aged 47 years. In the part of the wall, near the liver, "aberrant" biliary ducts with their characteristic concentric connective tissue are shown. Portion of a liver lobule is shown in the upper part of the illustration. (x 80)

The ducts frequently occur near the neck of the gall-bladder but may be found at any part along the main body as far as the fundus. When discovered in one section they may be followed by serial sections and this is particularly easy if the plane of the section happens to be longitudinal rather than transverse to the ducts (Fig. X). Often they run a tortuous course (Fig. XI).

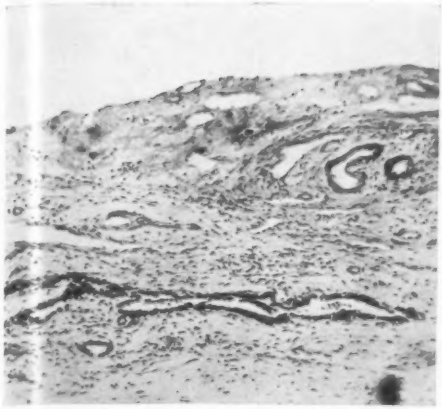

FIG. X. Photomicrograph of portion of the sub-peritoneal layer of the wall of a gall-bladder showing portion of an "aberrant" biliary duct cut longitudinally. The characteristic histological form of the epithelium is well shown. (x 80)

These ducts, particularly those in the region of the liver parenchyma, have a well-defined concentrically arranged cellular connective tissue layer (Fig. IX). Although some of the ducts near the liver are slightly dilated most of them have a small lumen (about 0.3 mm. in diameter) and they do not appear to show the dilatations which occur so frequently with the sinuses communicating with the gall-bladder lumen.

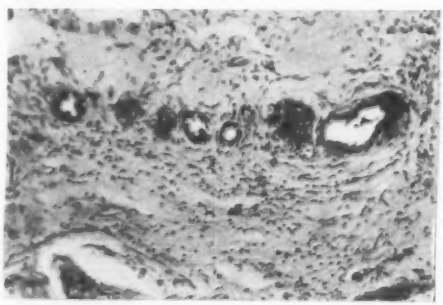

FIG. XI. Photomicrograph of portion of the wall of the gall-bladder showing a tortuous "aberrant" biliary duct cut longitudinally. (x 80)

The cells lining the ducts are cuboidal in form, are somewhat less regular than the cells lining the crypts and the nuclei, though regular in size and shape, are less regular in their relation to the basement membrane than those of the gall-bladder cells. Their resemblance to the cells of the intra-hepatic bile ducts is striking and there is seldom any question of confusion between these and the gall-bladder glands or sinuses proper.

These ducts may be found in the gall-bladders of young infants but they are also found in adults of middle age. As with many other conditions in the body it has been assumed that these structures have developed during foetal life as the result of some aberrant development of the embryonic primordium of the liver. In this regard it must be remembered that in infants islets of liver tissue are to be found in the peri-muscular layer of the gall-bladder wall. On the other hand such remnants of liver tissue are rare in the adult, whereas ducts of this kind may be found in as high as 10 per cent. of cases examined.

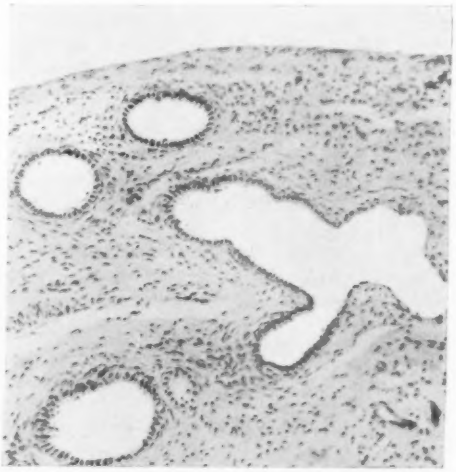

FIG. XII. Photomicrograph of portion of the sub-peritoneal layer of a gall-bladder showing glands of the mesothelial type. Glands were not found in the muscle layer despite extensive search. The regular cuboidal form of the epithelium (resembling that seen in other "peritoneal" glands) is shown. (x 80)

Although adequate information is lacking on which to form a complete judgement it seems likely that stimuli which will cause the proliferation and downgrowth of an epithelium of the mucous membrane of the

gall-bladder into the wall may also act similarly on the bile ducts which are present in the gall-bladder fossa.

Sub-Peritoneal (Mesothelial) Glands

Glandular structures in the sub-peritoneal coat, different both from those of the sinuses and of the bile ducts, may sometimes be seen (Fig. VIIIC). They are recognized at first by their very clear-cut and different histological form.

The spaces have a larger lumen than the bile ducts and the cells lining them are clearly cuboidal in shape presenting a "diagrammatic" appearance. Both the nuclei and the protoplasm stain rather more lightly than the corresponding cells of the other types (Fig. XII). Furthermore, these glands resemble those observed in other parts of the peritoneum.

When observed, they are quite localized and cannot be followed by serial section either to the adjacent liver or deeply into the muscle coat towards the lumen. Occasionally they may be in contact with the peritoneal layer but often are separated from it.

When there are numerous downgrowths from the mucosa of the gall-bladder into the subjacent tissues with the development of numerous types of epithelium, the unequivocal segregation of the mesothelial glands from the glands of the sinuses may present some difficulty. However, when such downgrowths are absent their position and characteristic cytological structure makes their diagnosis easy.

DISCUSSION

Epithelium-lined structures in the wall of the gall-bladder are found commonly in organs removed surgically. They are now well known and do not present difficulties in interpretation or in differentiation from neoplastic conditions.

They occur in three distinct forms (Fig. VIII): one in which the glands are to be found in the muscle layers and indeed in all the coats, and the others in which these are found only in the sub-peritoneal coat. Thus in the sub-peritoneal layer glands of three different and distinct kinds may be encountered.

The form in which the glands are found in all layers and in which they communicate with the lumen of the gall-bladder is the best known and is indeed, the most important. It occurs in several different macroscopic guises and, in addition, histologically the glands may show various types of intestinal epithelium ranging from tall columnar epithelium of the small bowel type to that of gastro-duodenal or pancreatic glands. The other forms have characteristic types of epithelium, one being of the intra-hepatic biliary type and the other of a characteristic "mesothelial" form.

These different kinds of glands in the sub-peritoneal coat have quite a different clinical significance. In the case of the sinuses, their continuity with the cavity of the gall-bladder allows biliary contents to be present in the sub-peritoneal layer and it has been suggested that rupture of a sub-peritoneal dilated gland, which may be almost or quite impossible to find on macroscopic examination, can result in spilling of bile into the peritoneal cavity with a resulting bile peritonitis. Infection may also spread through the wall of the gall-bladder in some cases more rapidly than it does in others. Furthermore, the necrosis which sometimes affects the submucous layer of the gall-bladder in some infections may spread to the deeper layers of the wall of the gall-bladder by way of the crypts and thus produce localized gangrene of the wall.

The aberrant bile ducts are of relatively little clinical importance. It is known that leakage may occur from biliary ducts in the gall-bladder fossa after cholecystectomy, particularly from large ones which communicate with the body of the gall-bladder itself; but these seldom give trouble. The small ducts that have been described here have such a minute lumen that any leakage from them is likely to be quite insignificant. It could not be of the same order of leakage that can occur from the sometimes widely dilated sinuses which communicate with sub-peritoneal glands.

The large accessory bile ducts which pass from the body of the gall-bladder into the liver by way of the gall-bladder fossa can

be regarded as greatly enlarged "aberrant biliary ducts" and thus as constituting an exception to the statement that "aberrant ducts" never communicate with the gall-bladder lumen. However, this does not affect the observation that the small ducts, in fact, are confined to the sub-peritoneal coat and do not communicate with the lumen.

The glands of peritoneal origin are of pathological rather than surgical importance though they may be part of a general group involving a wide peritoneal area and may occasionally, when dilated, give rise to diagnostic difficulties.

Regarding terminology, it is clear, from what has been said, that the eponymous terminology that has been applied to these structures is thoroughly unsatisfactory. The sinuses were all described by Rokitansky, Luschka and Aschoff, amongst others and, in view of the eminently satisfactory and clear description of Luschka, it seems ungracious to refer to these as the Rokitansky-Aschoff sinuses alone. Incidentally it has been the custom for many years to refer to them as the Luschka sinuses and the writer on previous occasions (1931, 1934), following the original description of Luschka, referred to them by the name of Luschka's glands.

On the other hand, Luschka certainly did describe the sub-peritoneal bile ducts and appreciated their significance. Since this was not appreciated by many writers, even including Aschoff, it is only right, if we are to adopt an eponymous terminology at all, that we should give these ducts Luschka's name. Thus it would be desirable to call the sinuses Rokitansky-Aschoff or Luschka sinuses, and the ducts Luschka ducts. If we avoid eponyms, whether they should be referred to as "aberrant" bile ducts or hyperplasia of the bile ducts will, of course, be determined by one's attitude as to whether any phenomenon of uncertain aetiology is likely *a priori* to arise in the congenital or developmental period (a point of view that has been of very wide acceptance over the last century) or is more probably due to tissue changes occurring at about the time when they are observed.

The mesothelial glands are of interest principally to the pathologist and what problem may present is one of differentiation from the other two types.

The two secondary phenomena—the distension of crypts to form cysts and diverticula and intra-mural calculi—are of importance principally because these may be diagnosed before operation. Provided that their general features are recognized, it may be possible to visualize these small crypts when they are filled with dye during cholecystography. Of course, it is necessary that the gall-bladder should be functioning sufficiently well to concentrate the dye; that the diagnosis has been made so seldom so far by this means may be due to the frequent association of disturbances of gall-bladder function with these changes in the wall.

Similarly a peripheral distribution of some calculi in relation to either concentrated dye in the cavity of the gall-bladder or a stone or a collection of stones in the cavity of the gall-bladder may enable the diagnosis of mural calculi to be made.

Localized thickenings of the wall of the gall-bladder and sometimes a projection on the peritoneal surface such as is seen in the specimen illustrated in Fig. II will allow the surgeon (or, as it was in the case shown, the pathologist) to make the diagnosis of mural calculi before the gall bladder is opened. The presence of calculi in this situation, of course, enables the diagnosis of sinuses in the wall (cholecystitis glandularis) to be made with certainty.

SUMMARY

Epithelium-lined spaces are found in the wall of the gall-bladder and often in the sub-peritoneal coat.

These are of three distinct types which have different origins:

(a) Sinuses communicating with the lumen of the gall-bladder;

(b) Ducts communicating with intra-hepatic ducts but not with the gall-bladder;

(c) Sub-peritoneal glands of mesothelial origin.

The sinuses (Rokitansky-Aschoff sinuses or cholecystitis glandularis) have a wide field of macroscopic form ranging from those in which the organ is relatively normal and there are only a few crypts to various localized or diffuse thickenings of the wall.

They are important because of various complications such as cyst formation and development of intra-mural calculi. Rupture of sub-peritoneal cysts may give rise to choleperitoneum.

The ducts, commonly seen on the hepatic aspect of the organ, may occur in the sub-peritoneal zone. They never communicate with the lumen of the gall-bladder and they have a characteristic histological structure.

The mesothelial glands also have a characteristically different histological structure and are of importance mainly in so far as they have to be distinguished from the others previously described.

ACKNOWLEDGEMENTS

I am indebted to Dr. J. Perry for specimens shown in Figs. III and VII and also to Mr. R. Inglis, Photographer, Royal Melbourne Hospital, for some of the photographs.

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PAGET'S DISEASE OF THE NIPPLE

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SINCE Sir James Paget, in 1874, described the lesion of the nipple which now bears his name, an extensive literature has accumulated on the subject. In point of fact the earliest clinical description of the surface lesion was that given by Velpeau in 1840. It remained, however, for Paget to discover the intimate association of the epidermal lesion with the occurrence of a mammary carcinoma, and to establish our present concept of the condition which therefore justifies the eponymous terminology.

Paget observed 15 cases of chronic affections of the epithelium of the nipple and areola and noted that they were succeeded by the development of a carcinoma in underlying breast tissue. This, he said, occurred usually within one or two years of the appearance of the skin lesion. The nature of the skin lesion was variable — in the majority of his cases it presented "the appearance of a florid, intensely red, raw surface, very finely granular, as if nearly the whole thickness of the epidermis were removed." In some, however, it presented the appearance of a chronic eczema, in others it resembled psoriasis.

It is to be noted that, on clinical grounds, Paget described carcinoma of the breast as following a cutaneous lesion.

Butlin in 1876 recorded the earliest histological studies of this condition. He believed that he could demonstrate a direct relation between the surface lesion and that deep in the gland, and inferred that the surface lesion was primary and the deeper lesions secondary in nature.

Thin, in 1881, was first to advocate that the surface lesion in Paget's disease is secondary to a carcinoma in the underlying breast. This paper marked the beginning of a prolonged controversy as to the site of origin of Paget's disease of the nipple.

Darier aroused great interest in the subject when, in 1899, he announced that Paget's disease was due to "psorosperms." After further studies, however, he decided that the abnormal cellular elements, described by him as coccidia, were in fact nothing more than epithelial cells which had undergone a special kind of degeneration to which he applied the term *dyskeratose*.

Darier, then, was first to describe "Paget" cells and he maintained that they were malpighian cells which had undergone developmental segregation and had subsequently developed in an abnormal fashion, independent of their neighbours.

This view was strongly attacked by Pautrier (1928) who stated that Paget cells are truly neoplastic, with power to invade, and not merely abnormal epithelial cells.

The precise nature and origin of these peculiar cells became the subject of active polemics. Some maintained that they were purely epidermal in origin, arising solely in the epithelium of the nipple. Amongst these authors further difference of opinion existed, some maintaining that the cells were of degenerate nature, others that they were in fact neoplastic cells arising *in situ*.

The alternative school maintained that Paget cells arose in the epithelium of the ducts of the breast and subsequently migrated into the epithelium of the nipple where they were observed as typical Paget cells.

Table 1

HYPOTHESES OF ORIGIN OF PAGET CELLS

(a) Epidermis:	(i) Degenerate epidermal cells (ii) Neoplastic epidermal cells
(b) Ducts:	Neoplastic cells which invade epidermis

TABLE 2

A SUMMARY OF DETAILS OF THE TWENTY CASES REVIEWED

This is derived from a survey of case histories and is mainly self-explanatory

Case	*Age*	*Duration*	*Presenting Symptom*	*Side and Size*	*Nature of Discharge*	*Macroscopic Description*	*Lump in Breast*	*Nodes*	*Metastases*	*Microscopic Description*	*Treatment*	*"Follow Up"*	*Remarks*
1 (E.O.)	45	6 mths.	Nipple lesion	Left. Nipple and areola involved	Serous	Moist, red, granular	–	–	–	Nipple + Ducts + Breast –	Mastectomy	10 yrs. Alive and well	
2 (A.G.)	45	7 weeks	Nipple lesion	Left. 3 cm. diam. around nipple	Nil	Dry, scaling	–	–	–	Nipple + Ducts – Breast –	Mastectomy	5 yrs. Alive and well	Had associated lobular hyperplasia
3 (C.C.)	60	12 mths.	Nipple lesion	Right. Limited to nipple	Serous	Red, thick, tender	–	–	–	Nipple + Ducts + Breast –	Radical Mastectomy	5 yrs. Alive and well	
4 (L.M.)	61	9 yrs.	Nipple lesion	Right. 10 cm. diam. around nipple	Purulent	Eroded, red, ulcerated, weeping	5 cm. diam. Mobile	+	–	Nipple + Ducts + Breast + Lymph Nodes } +	Radical Mastectomy	Died within 1 year	P.M. showed extensive secondary carcinoma
5 (A.O.)	50	3 yrs.	Nipple lesion	Right. 2.5 cm. diam. around nipple	Nil	Dry, red, scaling	5 cm. diam. Mobile	–	–	Nipple + Biopsy only	Radiotherapy	Died within 6 yrs.	P.M. showed extensive secondary carcinoma
6 (J.B.)	72	6 yrs.	Nipple lesion	Left. 9 x 6 cm. around nipple	Blood-stained	Eczematous, scaly, weeping	–	–	–	Nipple + Biopsy only	Radiotherapy	3 yrs. Alive and well	
7 (A.C.)	59	6 mths.	Nipple lesion	Left. 3 cm. diam. around nipple	Serous	Red, raw, weeping	+	–	–	Nipple + Ducts + Breast + Lymph Nodes } –	Radical Mastectomy	4 yrs. Alive and well	
8 (S.C.)	82	1 year	Nipple lesion	Right. Extensive	Present: not described	Red, weeping granular	+	+	+	Nipple + Biopsy only	Radiotherapy	Died within 1 year	P.M. showed extensive secondary carcinoma. Bone deposits when first seen
9 (M.M.)	56	4 mths.	Nipple lesion	Left. Limited to nipple	Present: not described	Red and ulcerated	+	–	–	Nipple + Ducts + Breast + Lymph Nodes } –	Radical mastectomy. Radiotherapy	6 yrs. Alive and well	
10 (D.H.)	38	1 year	Nipple lesion	Right. Nipple and areola involved	Serous	Red, raw, ulcerated	+	–	–	Nipple + Ducts + Breast + Lymph Nodes } –	Radical mastectomy. Radiotherapy	1 year. Alive and well	Only short period has elapsed since treatment
11 (M.F.)	72	6 mths.	Nipple lesion	Right. Nipple and areola involved	—	Red and ulcerated	+	–	–	Nipple + Ducts + Breast + Lymph Nodes } +	Radical mastectomy. Radiotherapy	1 year. Alive and well	Only short period has elapsed since treatment
12 (G.G.)	59	6 mths.	Lump	Left. Limited to nipple	Nil	Dry, scaling	4 cm. diam. lower outer quadrant	+	–	Nipple + Ducts + Breast + Lymph Nodes } +	Radical mastectomy		Patient noticed lump three weeks before skin lesion
13 (A.C.)	58	1 year	Nipple lesion	Right. 1 cm. diam. on nipple	Yellow, serous exudate	Raised, red, granular	3 cm. diam. upper outer quadrant	–	–	Nipple + Ducts + Breast +	Radical mastectomy		
14 (M.I.)	61	4 mths.	Discharge from nipple	Right. Limited to nipple and areola	Blood-stained	Red, raw, oozing	2 cm. diam.	–	–	Nipple + Ducts – Breast – Lymph Nodes } –	Radical mastectomy	2 yrs. Alive and well	Tumour in breast proved to be non-malignant

TABLE 2—(continued)

Case	Age	Duration	Presenting Symptom	Side and Size	Nature of Discharge	Macroscopic Description	Lump in Breast	Nodes	Metastases	Microscopic Description	Treatment	"Follow Up"	Remarks
15 (C.P.)	52	18 mths.	Nipple lesion	Right. Limited to nipple	Blood-stained	Red and ulcerated	+	+	−	Nipple + Ducts + Breast + Lymph Nodes −/+	Radical mastectomy	10 yrs. Alive and well	Glands, thought clinically to be involved, showed inflammation
16 (M.K.)	46	1 year	Lump	Right. Limited to nipple	Blood-stained	Red, raw, weeping	+	+	−	Nipple + Ducts, none seen Breast + Lymph Nodes +/+	Radical mastectomy		Also had carcinoma in left breast treated by radical mastectomy
17 (F.W.)	46	2 yrs.	Discharge from nipple	Left 4 cm. diam. around nipple	Present: Not described	Red, weeping area	+	−	−	Nipple + Ducts + Breast + Lymph Nodes +/+	Radical mastectomy		These glands clinically clear, contained carcinoma
18 (G.V.)	49	2 yrs.	Discharge from nipple	Right. Nipple and areola involved	Blood-stained	Red, weeping	+	+	−	Nipple + Ducts + Breast +	Radical mastectomy	Died within 2 yrs.	In this case break away from duct wall occurred immediately under nipple
19 (A.T.)	77	8 yrs.	Nipple lesion	Right. 0.5 cm. diam. on nipple	—	Ulcerated	−	−	−	Nipple + Biopsy only	Mastectomy	1 year. Alive and well	Had three previous applications of radium. See text
20 (C.L.)	72	2 yrs.	Nipple lesion	Left. Limited to nipple	—	Dry and ulcerated	+	−	−	Nipple + Ducts − Breast −	Mastectomy		Section showed tumour resembling epithelioma under nipple. Paget cells in epithelioma

Clinical presence of a tumour, nodes and metastases are indicated by +

Microscopic description:

Nipple	+	typical Paget cells were seen.
Ducts	+	carcinomatous infiltration of duct wall was seen.
Ducts	−	ducts were clear.
Breast	+	presence of a *microscopically* diagnosed carcinoma.
Breast	−	a clear breast.
Nodes	+	presence of carcinoma cells in the nodes.

It might be supposed that careful study of cases of extra-mammary Paget's disease would clarify the problem. These studies (Cheatle and Cutler, 1931) support the view that Paget cells are in fact neoplastic but fail to give a lead as to their site of origin because, in most cases, extra-mammary Paget's disease is associated with an underlying carcinoma, often arising in sweat glands.

Muir (1934) stated that both the breast carcinoma and the nipple changes are secondary to an established intra-duct carcinoma. In this paper he gave excellent illustrations of anaplastic carcinoma cells spreading in the epithelium. Inglis (1936) studied cases of Paget's disease by the technique of cutting large sections of nipple and breast. He maintains that the initial lesion is in the ducts of the breast. Spread from this lesion may occur in two directions: that is, upwards into the epithelium where Paget cells will be seen, or down into the ducts, ultimately to break out into the breast tissue, there to produce a carcinoma.

This process may occur at quite different rates in these two directions so that either Paget's lesion of the nipple or mammary carcinoma may be the initial symptom.

Recently Dockerty and Harrington (1951) reported 7 cases of carcinoma of the breast where section of a macroscopically normal nipple had revealed microscopically deposits of Paget cells. These authors suggest that

the cutaneous lesion is secondary to an established carcinoma in the underlying breast.

The present series consists of cases of Paget's disease of the nipple derived from various sources and treated in Melbourne over the last twenty years. A group of 20 cases has been collected and analyzed with respect to various features.

Age and Sex

Incidence of the condition was confined to the female breast. The average age is 57 years—the youngest being 38 and the oldest 82. It would appear that Paget's disease presents a similar age distribution to that seen in mammary carcinoma in general.

Initial Symptom

In 15 cases the earliest complaint made by the patient was that of a visible lesion on the nipple. In 3 cases a discharge from the nipple was the presenting symptom, whilst in 2 cases a lump in the breast was the first indication of disease.

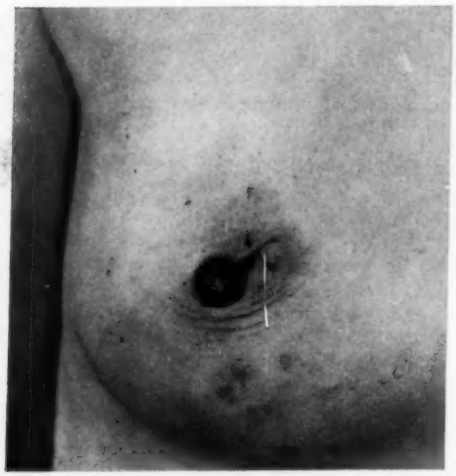

FIG. I. Photograph of a patient showing a relatively early lesion of the nipple and areola. An incision from which a biopsy has been taken is clearly visible (Case 7).

It may be noted at this point that, although 15 cases were found to have a palpable lump in the breast when first examined, only 5 of them were aware of its presence. Of these 5 cases only 2 had observed that the appearance of a lump preceded the cutaneous lesion. In the remaining 3 cases the lump was noticed six, eighteen and twenty-one months after skin changes were seen.

Duration of History

The duration of history varied greatly, the longest being nine years and the shortest seven weeks. In a small series such as this and in view of such wide variation, an average time would be meaningless. On surveying Table 2, however, it would appear that in most cases the lesion had been present for six to twelve months before the patient sought medical advice.

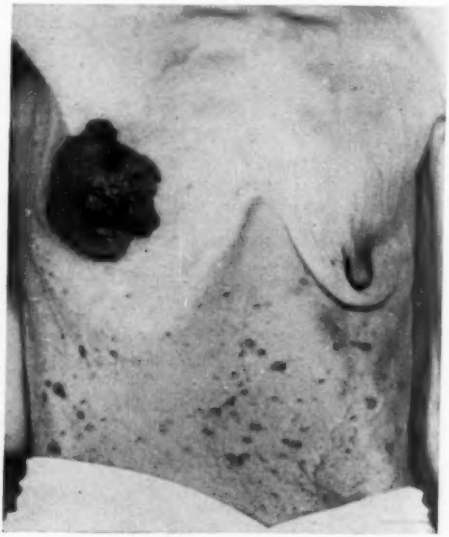

FIG. II. Photograph of a patient showing a neglected lesion. Extensive involvement of the skin of the breast is seen. This lesion had been progressing for nine years (Case 4).

Side and Size of Lesion

The disease was observed to affect the left nipple on 8 occasions and the right on twelve. The size of the lesion varied considerably as may be seen in Table 2. However, in the majority of cases advice was sought whilst the lesion was limited to the nipple and alveola (Fig. I). Only in neglected cases was a wider area of epithelium involved as may be illustrated by Case 4 in which the lesion had spread to involve an

area of skin 10 cm. in diameter around the nipple. This had been progressing for nine years (Fig. II).

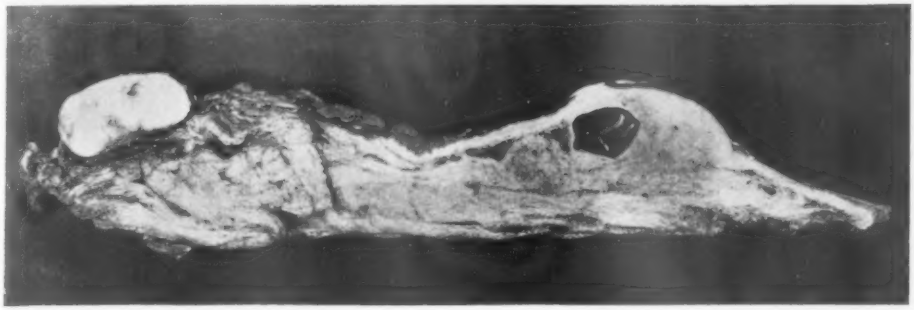

FIG. III. Photograph of a section of the operative specimen removed from Case 4 (Fig. II) showing involved skin, a carcinoma in the underlying breast, and an enlarged lymph node.

Clinical Appearance

On presentation for treatment all cases in this series were observed to have a lesion of the epithelium of the nipple, surrounding areola and sometimes the surrounding skin.

In 13 cases the description was of a red, raw, granular lesion which discharged either a purulent or sanguineous exudate. In 3 cases the lesion was eczematous with small, yellow vesicles and incrustations and in four cases the terms dry and scaling were applied to the lesion.

Macroscopic Appearance

After removal the specimens show the epithelial changes already described. In addition a carcinoma may be seen in the underlying breast ranging in size from a minute nodule up to 5 cm. in diameter. Axillary lymph nodes may also be involved (Fig. III).

Microscopic Appearance

Microscopically all cases show typical Paget cells (Fig. VI). These are large clear cells situated in the epidermis. The cytoplasm is plentiful and vacuolated, and their nuclei, small and dark-staining, may be peripheral and crescentic or central and rounded.

The earliest stage can be seen at the edge of the lesion (Fig. IV). Here single Paget cells are scattered throughout the epithelium. Initially the amount of cytoplasm is small, but it enlarges and as it does so, groups of Paget cells coalesce to form spaces in the epithelium (Fig. V).

These spaces now run together and the superficial layers of the epithelium are shed leaving a layer of prickle cells and Paget cells forming the base of the lesion. This layer of cells varies considerably in thickness.

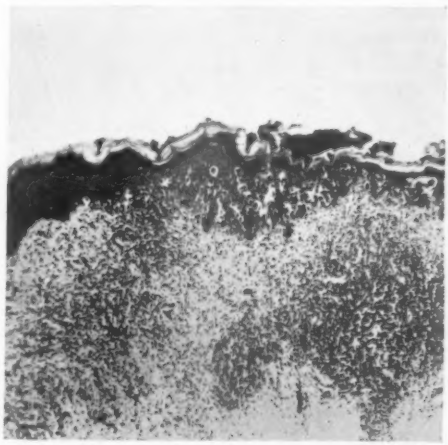

FIG. IV. Photomicrograph of a section taken from the edge of a typical skin lesion (Case 7). Paget cells are to be seen in the affected epidermis. (x 50)

Associated with the process described above, inflammatory changes may be observed in the underlying connective tissue. These take the form of infiltration with polymorphs, macrophages and small round cells. In some situations the superficial epithelium is lost completely and it is in these situations that wandering cells collect most densely.

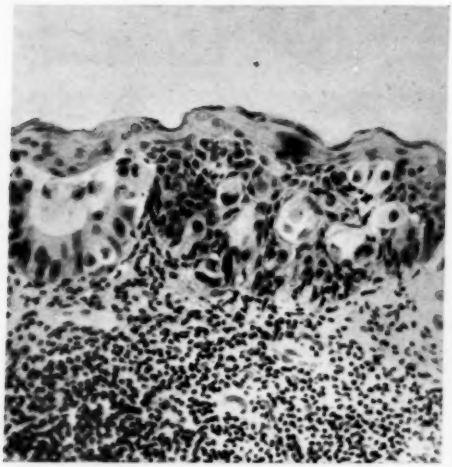

FIG. V. Photomicrograph of a section taken from a skin lesion, showing Paget cells in groups and inflammatory cells collected in the dermis (Case 6). (x 200)

It must be emphasized that there is no evidence seen of the Paget cells invading the underlying dermis, all cells collected in that area being of connective tissue type.

When the ducts are examined it is found that typical Paget cells do not occur in this region. The neoplastic cells spread in the duct wall either between layers of epithelial cells or between epithelial cells and basement membrane of the duct. This results in the epithelium becoming heaped up and irregular in involved ducts (Fig. VII). In some cases the ducts were seen to be completely filled with proliferating carcinoma cells. As is observed in the skin, inflammatory changes may occur around involved ducts.

In this series duct involvement was observed in 12 cases. Clear ducts were noted in three cases and no duct was present in the material available in five cases. No conclusion can be drawn from these figures, however, because in no case was an exhaustive examination of all ducts carried out.

The extent of the duct involvement varied considerably, in some cases, only superficial ducts were involved, in others extensive intraduct spread was observed.

Break away of carcinoma cells from the ducts was observed in different situations (Fig. VIII). In some cases it could be seen immediately under the nipple, in others deep in the gland.

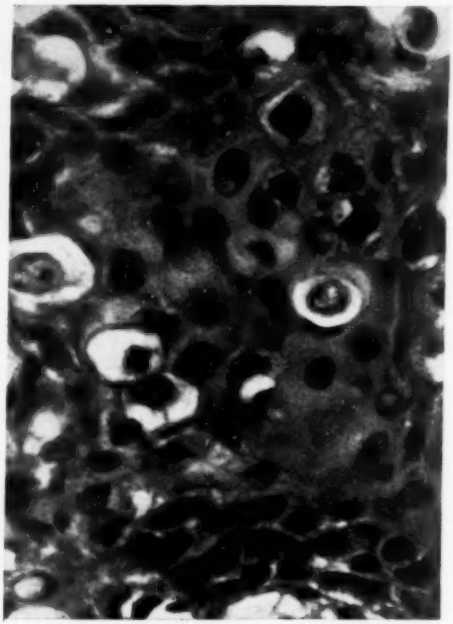

FIG. VI. Photograph of an area of epidermis in which are Paget cells with clear vacuolated protoplasm (Case 4). (x 700)

Two points seem fairly clear from examination of the material:

(a) it would be clinically impossible to detect early cases of spread of carcinoma cells from the duct wall;

(b) this invasion may occur at several points in the one specimen.

The carcinoma in the underlying breast when present showed no unusual features. Some lymph node metastases were observed —these again were in no way remarkable.

Associated Lesions

(a) Carcinoma in breast: In 15 cases a lump was noticed clinically at initial examination. All were diagnosed as carcinoma.

One of these (Case 14) subsequently proved microscopically to show lobular hyperplasia, leaving three quarters of the cases to show the presence of a carcinoma in the breast on presentation for treatment.

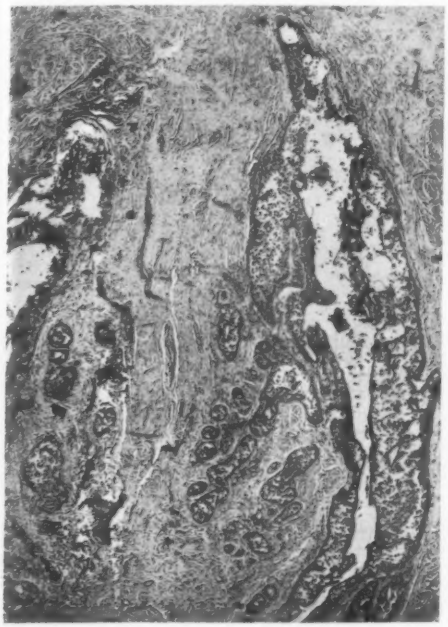

FIG. VII. Photomicrograph of a section of breast showing large ducts which are lined by carcinoma cells; there is also an area of invasion of breast tissue (Case 7). (Compare Fig. VIII) (x 25)

(b) Lymph node involvement: This was detected clinically in 6 cases and in all it was considered to be due to neoplastic infiltration. In one of these, however, section showed merely reactive changes. In two cases microscopical deposits were observed in glands clinically considered to be clear. In no case was there involvement of nodes without a demonstrable carcinoma in the breast.

(c) Distant metastasis: This was seen only in one case—secondary tumours being discovered in bone.

Treatment

In this series 3 cases were treated with deep-ray therapy alone; 2 cases were treated by simple mastectomy and the remaining 15 cases by radical mastectomy, some followed by post-operative radiotherapy. Case 19 deserves further mention. When first seen a nipple lesion had been present for four years and had temporarily healed following two applications of surface radium. A biopsy on this occasion showed typical Paget's disease and deep therapy was instituted. Again healing occurred. Three years later, however, the lesion had recurred and was larger than ever. The breast was clear and no axillary nodes were palpable. At this stage a simple mastectomy was performed; unfortunately the specimen was not available for examination.

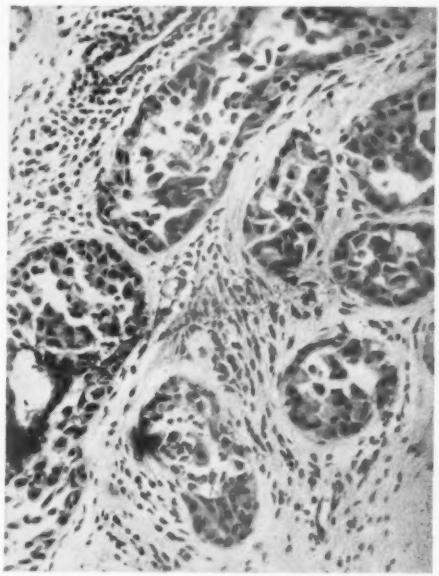

FIG. VIII. Photomicrograph of the same section as Fig. VII showing the characters of the carcinoma cells which are invading the breast tissue (Case 7). (x 150)

"Follow-up"

In only 15 cases could the subsequent history of the patient be traced, thus only these will be considered under this heading. It would seem that the cases fall into three groups:

(a) those in which only the epithelium of the nipple and ducts were involved (six cases), all had survived for a period ranging from one to ten years;

(b) those in which a carcinoma of the breast was present but lymph nodes were not involved (six cases), two had died from carcinoma of the breast;

(c) those in which lymph nodes were involved by carcinoma (three cases), only one of which had survived for more than one year.

DISCUSSION

On reviewing this series it is seen that the initial complaint of a patient suffering from Paget's disease is usually that of a lesion in the epithelium of her nipple. She may, however, have noticed that either a lump or a discharge from the nipple preceded the occurrence of a surface lesion. Both may be an indication of the presence of an intraduct carcinoma. By the time medical advice is sought the lesion has usually spread to involve nipple and areola and a period of from six to twelve months has elapsed.

Such a patient, on presenting for examination, will show a palpable carcinoma of the breast in 75 per cent. of cases. Should a tumour be present, then the treatment and prognosis obviously depend on the presence and nature of that tumour, rather than on the presence of superficial changes.

The problem occurs in the remaining 25 per cent. of cases without a palpable tumour. It has been noted that wide-spread duct involvement may be present in a breast declared clinically clear, and in one such case recurrence followed three attempts at therapy directed to the nipple alone. It has also been pointed out that it is impossible to detect early invasion of the breast from involved ducts, and therefore it seems reasonable that a case of Paget's disease of the nipple without an associated breast tumour should be treated in the same fashion as any other mammary carcinoma.

The subsequent history of these patients indicates that treatment instituted in a case showing only superficial changes gives a much better result than in those where a mammary carcinoma was present when first seen.

Paget's disease of the nipple must be considered as a possible diagnosis in any lesion of the nipple which persists for longer than three to four weeks. In such a case, should the diagnosis be in doubt, a histological section will clarify the situation by showing the presence of typical Paget cells in the epithelium.

SUMMARY

(1) A group of twenty cases of Paget's disease of the nipple was collected and reviewed.

(2) A brief historical survey of the condition is given.

(3) Macroscopically, Paget's disease of the nipple may present a variable picture. In the majority of cases the lesion is red, raw and granular in appearance, but in others, it may be eczematous or dry and scaling. Paget's disease should be suspected when any nipple lesion persists for more than three to four weeks.

(4) Microscopically characteristic changes are seen. Typical Paget cells occur around the edge of the lesion, whilst centrally the superficial layers of the epidermis may be lost.

(5) Carcinoma is present in the underlying breast in 75 per cent. of cases when first seen.

(6) In those cases without a palpable tumour, treatment should be as for carcinoma of the breast.

ACKNOWLEDGEMENTS

I wish to thank the medical staff of the Royal Melbourne and Alfred Hospitals for permission to review their records; Mr. R. Inglis, Clinical Photographer at the Royal Melbourne Hospital, for the excellent macroscopic photographs; and Miss N. Bowman of the Almoner's Department, Royal Melbourne Hospital, for her aid in tracing many of the patients.

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CONGENITAL TRACHEO-OESOPHAGEAL FISTULA WITHOUT ATRESIA BUT WITH LARGE OESOPHAGEAL DIVERTICULUM

By Douglas Robb

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THIS case adds what is believed to be a fresh variation to the well-known series of congenital malformations in the upper and middle thirds of the oesophagus, most often encountered in new born infants.

Vogt's (1929) classification of cases with atresia is still very useful:—

Type 1 Complete absence of the oesophagus.

Type 2 Atresia with an upper and lower oesophageal segment each ending in a blind pouch.

Type 3 Atresia of oesophagus with tracheo-oesophageal fistula.

(i) Fistula between upper segment and trachea.

(ii) Fistula between lower segment and trachea.

(iii) Fistula between both segments and trachea.

Type 3 (ii) is the commonest—84 per cent. and 91 per cent. are reported in two sizeable series.

Holt, Haight and Hodges (1947) suggest adding another type—fistula without atresia—to this series, and this situation is described and illustrated by Swenson (1948).

The case about to be described presented the fistula without atresia, but in addition had a bulky diverticulum posteriorly, as though the lower segment, in attaching itself (successfully) to the upper segment did so not at its lower extremity but at a point some distance up its anterior surface, though still below the level of the fistula. A diagram illustrates the findings.

The diagnosis of fistula is best made with the patient in the prone position, which gives the lipiodol its best chance to enter the trachea, particularly as in the case to be described where the direction of the fistula was upwards from oesophagus to trachea.

FIG. I. X-ray photograph (barium swallow) showing diverticulum before operation. The fistula is not demonstrated.

Case Report

Gordon McP., 11 years, had attacks of choking from birth. After a meal he would cough, choke, and go blue, having to be watched night and day. Sitting him up and patting his back would help him. As he got older the attacks of choking got

less frequent and less severe but they still occurred, though he learnt to manage them himself. He developed normally and was satisfactorily nourished.

The pouch in the oesophagus was found at the age of 5, and at an earlier X-ray in another hospital there was said to be a communication between oesophagus and bronchial tree. On barium swallow the pouch was confirmed, beginning on the posterior wall 1 cm. above the tracheal bifurcation. No fistula to the trachea was demonstrated but lipiodol was not used nor the prone position.

FIG. II. X-ray photograph (barium swallow) showing gullet after repair of fistula and diverticulum.

Bronchoscopy by Mr. John Borrie showed a wide upper oesophagus. At 20 cm. the wide mouth of the pouch was seen posteriorly. The mucosa was normal and the pouch tapered to a point about 3.5 cm. lower down. The rest of the oesophagus was normal.

Operation

A right thoracotomy was done through the bed of the resected 5th rib (also 1 inch of the 6th rib at angle was taken) under endo-tracheal anaesthesia by Dr. J. Watt.

A bulky oesophagus was seen under the pleura above the azygos vein which was divided and the pleura was incised vertically. There was a lot of oozing around the oesophagus which seemed of normal outside appearance below the level of the azygos vein, but wider and more muscular above. There was a suggestion of a line of demarcation between diverticulum, which was posterior and tapered to a point, and the main oesophagus, and this proved to be so, but essentially the upper part looked like a thick, single tube.

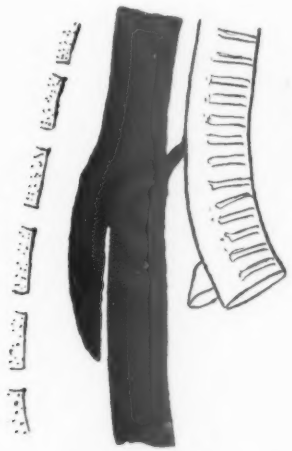

FIG. III. Diagram showing oesophagus with posterior pouch and fistula to trachea.

A vertical postero-lateral incision through muscular and mucous linings showed that the pouch had been entered. It was 3.5 cm. long from its lower tip to the semilunar fold over which one could pass a probe into the main gullet channel. About 1 cm. above the fold, on the anterior wall, there was a dimple containing a fleck of white material, and this could be probed in an upward direction with a coarse probe for 3 or 4 cm., thereby causing tracheal irritation. There was thus no doubt about the fistula, and dissection between trachea and oesophagus revealed it. When divided, an oval hole in oesophageal mucosa 3 mm. long, and a slightly larger one 4 mm. long in the posterior wall of the trachea were seen. The anaesthetist's balloon on the endo-tracheal tube could be seen, and was avoided in the suturing. These holes were sutured with fine silk on atraumatic needles and in

each case a bundle of muscular and other adventitious tissue found and sutured over the mucosa to reinforce it. Neither recurrent laryngeal nerve was seen and both cords moved well afterwards.

The diverticulum was reduced by excision of excessive mucosa and interrupted fine silk sutures with knots in the lumen, closed the mucosa in a vertical line. Two layers of interrupted muscular sutures completed the closure.

The chest cavity was washed out with acriflavine solution, penicillin and streptomycin solution was left in, and the chest closed save for two tubes to underwater seals.

Convalescence was uneventful. A film taken of a barium swallow three weeks after the operation is shown.

SUMMARY

What is believed to be a rare variety of congenital oesophageal abnormality is described and a case history given. There was a fistula between trachea and oesophagus, no oesophageal atresia, and a large posterior oesophageal pouch. Surgical correction gave a good result.

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CAROTID BODY TUMOURS

A STUDY OF THREE CASES INCLUDING A BILATERAL EXAMPLE

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TUMOURS of the carotid body or glomus are uncommon, only four cases having been described in Australia (Edye, 1922; Starr *et alii*, 1944; Wyndham, 1947) and less than 300 cases recorded in the world literature to the end of 1950. In this paper four examples of carotid body tumours, which were operated on by Melbourne surgeons during the last fifteen years, are presented.

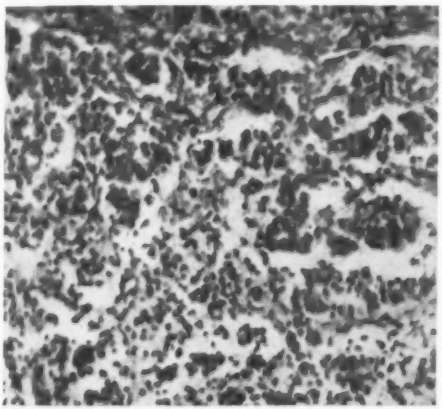

FIG. I. Photomicrograph of a section of the tumour from Case 1 showing groups of polyhedral cells separated by vascular connective tissue. (x 150)

One case, of particular importance, had bilateral tumours which were successfully excised during a single stage operation by the late Sir Alan Newton. At his instigation the patient was investigated during her convalescence, in an attempt to detect any change in the respiratory and circulatory systems following operation. It had been his intention to publish this case and it is felt that, because of the light they throw on the functions of the carotid bodies, the results of the investigations in this patient should not be left unrecorded.

Case Histories

Case 1

A female, aged 45, had observed a lump on the left side of her neck for several years. Recently there had been difficulty in swallowing, hoarseness and shortness of breath. There was a scar on the skin over the lump which she said was due to an exploratory operation some years previously when the removal of the mass was regarded as being too dangerous.

FIG. II. Photomicrograph of a section of the tumour from Case 1 showing sheets of tumour cells invading the adventitia of a blood vessel. (x 25)

At operation, a large vascular ovoid tumour, intimately attached to the carotid vessels at their bifurcation, was found. After a difficult dissection during which the left hypoglossal nerve, inextricably bound up with the tumour mass, was divided, the tumour was successfully removed. Post-operatively she had a temporary speech inpediment due to the loss of the hypoglossal nerve. The patient remained well till her death five years later, autopsy showing chronic nephritis and congestive cardiac failure. No recurrence of the tumour was found.

On pathological examination, after fixation, the tumour was found to be ovoid in shape and reddish-brown in colour. It measured 6 cm. in its greatest diameter (it had been larger apparently in the fresh state) and showed part of a large thin-walled vessel attached to the inferior pole and a small artery traversing it. The cut surface was a variegated reddish-grey colour.

Histologically, there was a network of closely packed capillaries separated by groups of cells arranged in alveolar fashion. The cell type was variable: some possessed nuclei with deeply-stained chromatin, others being pale and vesicular (Fig. I). The cytoplasm was eosinophilic; in some it was pale and vacuolated, whilst in others it was granular. The stroma was hyaline. The tumour was invading the adventitia of the large vessel (Fig. II).

Case 2

A female, aged 53, presented in 1940 with bilateral swellings which had been present in her neck for five years. The tumour on the right side had appeared first and had been associated with a "sore throat." Neither mass was enlarging rapidly. Her complaint was of a dull ache in her neck associated with hoarseness. Recently, she had been losing weight and felt very tired. A history of bilious attacks characterized by headache and occasional vomiting, present for most of her adult life, did not appear to be related to the swellings.

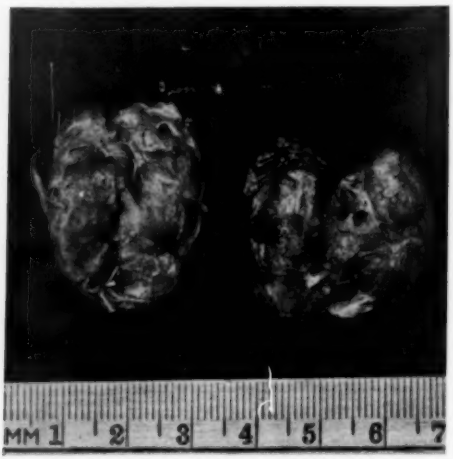

FIG. III. Photograph of the two tumours removed from Case 2. The ovoid tumour (on the left), is from the left side while the quadrangular tumour is from the right side. The posterior surfaces are presented to show the grooves from the carotid vessels.

On examination she was a thin, pale, little woman with very firm bilateral tumours below the angle of the jaw and deep to the upper third of the sterno-mastoid muscle. An examination of her ears, nose and throat showed no abnormality.

Sir Alan Newton advised surgical exploration of what were regarded as enlarged lymph nodes.

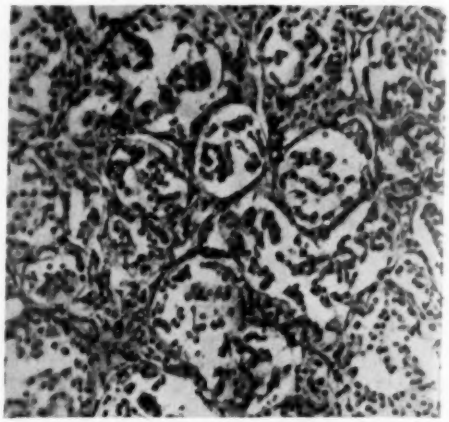

FIG. IV. Photomicrograph of a section of the tumour from the left side (Case 2). The tissue is alveolar in form, the alveoli containing polyhedral cells which have become slightly shrunken. There is only a small amount of connective tissue supporting the alveoli. (x 150)

At operation, vascular tumours about 1½ inches in diameter were found in the bifurcation of each common carotid artery (Fig. III); the right tumour was dissected out with some difficulty and ligation of the internal jugular vein was necessary on that side, while the left tumour was removed easily.

Post-operatively, she had a slight ptosis of the right eye and an evanescent paralysis of the right recurrent laryngeal nerve.

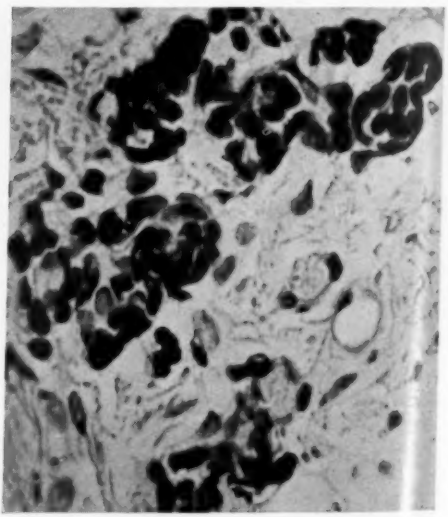

FIG. V. Photomicrograph of a section of the left-sided tumour (Case 2) showing the so-called "sympathogonia" cells with hyperchromatic nuclei. (x 350)

Pathological examination

The mass on the left side was a firm, nodular vascular tumour of irregular oval shape, apparently encapsulated and of light-brown colour. It showed a definite groove on its surface, measured 3.2 cm. x 2.5 cm. x 2.4 cm. and weighed 12.4 gm. Its cut surface was firm and fleshy with some minute lacunae visible and also dark-brown mottled areas due to haemorrhage.

Histologically, the fibrous capsule was very thin and in places ill-defined. Tumour cells were arranged in cords and clusters separated by many dilated sinusoidal capillaries. Also there were many alveoli loosely filled with cells (Fig. IV). The cells were mainly large, polyhedral, epithelium-like with a few of round and spindle shape and a very few multinucleated. The nuclei stained well and showed nucleoli.

The protoplasm in most cells was slightly granular although in some it was clear and homogeneous whilst in a few it was vacuolated. Cell borders in many cases were ill-defined. Some of the spindles were like plump endothelial cells. Clusters of small hyperchromatic poorly-differentiated round or oval nuclei could be seen between nests of parenchymal cells and alongside the sinusoidal capillaries. These cells were more numerous in the superficial portions of the tumour; these are classified by Chase (1933) as sympathogonia (Fig. V).

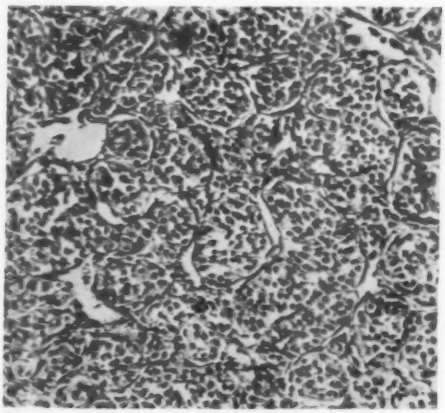

FIG. VI. Photomicrograph of a section of the right-sided tumour (Case 2). The tumour is composed of alveoli filled with polyhedral cells which are less shrunken than those in Fig. IV. There is a minute amount of connective tissue present while the vessels in the alveolar walls are sinusoidal in type. (x 150)

In some alveoli, prolongations from the tumour cells were apparently connected with the fibrous alveolar wall. The sinusoidal capillaries were numerous, many being dilated and lined by flattened endothelial cells. The tumour cells in many places were in close association with their outer wall.

Fibrous tissue surrounded most of the alveoli and was more abundant in the deeper portions of the tumour. It showed very few nuclei and was mainly collagen (Mallory's connective tissue and van Gieson's stains). In some areas a fine reticulum separated the individual tumour cells.

A few chromaffin cells were demonstrated chiefly lying in the stroma (methods used were [i] Schmorls [ii] T. and A. Ogata [iii] potassium bichromate with carmalum as a nuclear stain). Small collections of yellow-brown granules (altered blood pigment) were scattered throughout the tumour evidently vestiges of old vascular congestion and haemorrhage. Some neurofibrils were demonstrated.

The right sided tumour was roughly cuboidal, slightly nodular and of a light brown colour. It had a much deeper groove and measured 3 cm. x 2.9 cm. x 2.2 cm. weighing 10 gm. It was apparently covered by a thin fibrous capsule to which a few filiform fibrous tags were attached. The cut surface was similar to that of the left tumour.

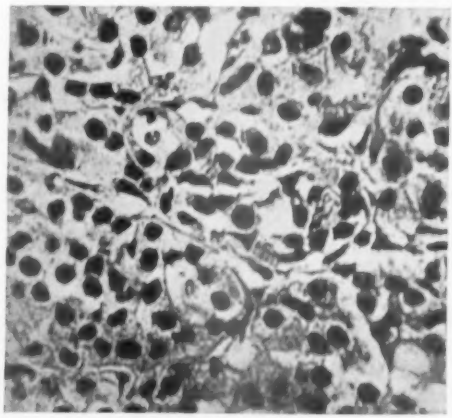

FIG. VII. Photomicrograph of a section of the right-sided tumour (Case 2) showing under higher magnification the cells with granular cytoplasm, arranged in alveoli. (x 350)

Histologically, alveolar formation was more evident in this tumour (Fig. VI), otherwise its structure was practically identical with that of the other. The tumour cells were similar in type, with well-staining nuclei and granular cytoplasm (Fig. VII). In most cases the cell limits were more clearly defined. Clusters of small hyperchromatic poorly-differentiated round or spindle nuclei could be seen as in the other tumour. These were again more numerous in the superficial portion of the tumour. Scattered granules of altered blood pigment were present in small quantities while chromaffin cells were demonstrated to be more numerous than in the first tumour. In places the fibrous stroma showed patchy lymphocytic infiltration. Some neurofibrils were present.

During the patient's convalescence Sir Alan Newton sent her for an investigation in which the respired air was varied in content.

The method of examination was to have the patient breathing from a reservoir containing oxygen and carbon dioxide at a given percentage in nitrogen. The expired air was recorded by a spirometer with record of time. The chest movements were recorded from a concertina tube stethograph and tambour with smoked paper.

Resting, the patient had an alveolar air concentration of 5.4 per cent. carbon dioxide and 14.3 per cent. oxygen. On breathing a mixture of gases containing 20 per cent. oxygen and 3 per cent. carbon dioxide, the breathing increased in volume from 8.4 litres per minute to 15 litres per minute. The alveolar air concentration of carbon dioxide had risen to 5.78 per cent. and the oxygen to 15.52 per cent. With a 6 per cent. carbon dioxide mixture, breathing increased to 28 litres per minute. With mixtures of 10 per cent., 8 per cent. and 7 per cent. oxygen and no carbon dioxide, breathing showed no response in the first four minutes on inspiring these mixtures but at the end of five minutes with the 7 per cent. oxygen there was some evidence of a slight increase in respiration from 8.4 litres per minute to 9.6 litres per minute. At this time, however, the patient was in a confused mental state and the alveolar air could not be obtained, because of a lack of co-operation by the patient. It is reasonable to suppose that the alveolar air oxygen concentration was somewhere below 7 per cent.

We may therefore conclude that in this patient with the alveolar oxygen concentration less than half the normal there was no response of the respiratory system to this oxygen lack but there was a response to an alveolar air concentration of carbon dioxide approximately 1/16 greater than the normal concentration. The threshold for increased respiration with increased carbon dioxide concentration of alveolar air was not, however, determined.

The blood pressure response to decreased oxygen in alveolar air was measured and showed no change at all, except that when the oxygen concentration in the alveolar air dropped below 7 per cent., the blood pressure dropped from 140/90 mm. of mercury to 120/85 mm. of mercury. There was no evidence of an increase in blood pressure in response to deficient oxygen supply.

The patient was alive and well one year later with no evidence of recurrence.

Case 3

A female, aged 33, presented in September, 1951, with a lump behind the left side of her jaw. This had been present for three years increasing slowly in size. Occasionally it had ached but had never been tender to the touch.

On examination, a mass, which was hard and deeply fixed was found behind the mandible on the left side. There was no pulsation and little if any mobility in any direction. The mass was not fixed to skin or sterno-mastoid muscle, which covered it posteriorly. Ears, nose and throat showed no abnormality.

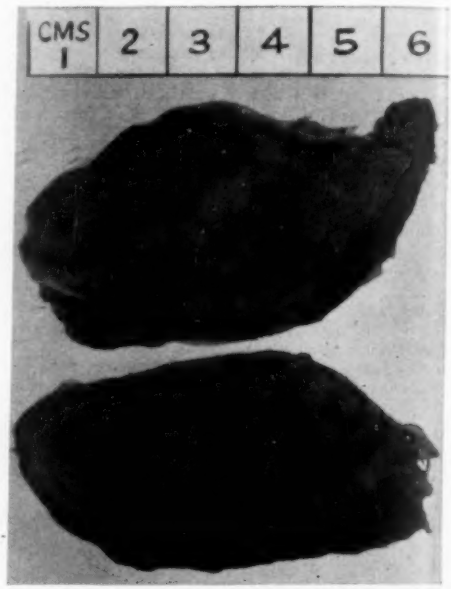

FIG. VIII. Photograph of the cut surface of the specimen from Case 3. Its variegated surface may be seen.

At operation, the tumour was found to embrace the bifurcation of the common carotid artery; it extended medially under the angle of the jaw and superiorly to the base of the skull. Posteriorly it rested on the transverse processes of the cervical vertebrae. By careful blunt dissection, the mass was separated from the carotid vessels but because of involvement in the tumour, the sympathetic trunk and the internal jugular vein had perforce to be ligated in the process. All carotid vessels remained intact, however.

During the operation, although the patient remained well oxygenated and of good colour, the pulse rate rose to 180 and remained there for some time before finally returning to about 130.

At the end of the operation the patient was noticed to have a constricted left pupil and a drooping left angle of the mouth. On recovery from the anaesthetic she suddenly developed an aphasia and a right hemiparesis both of which seemed to be improving until, on the second day, she suddenly died.

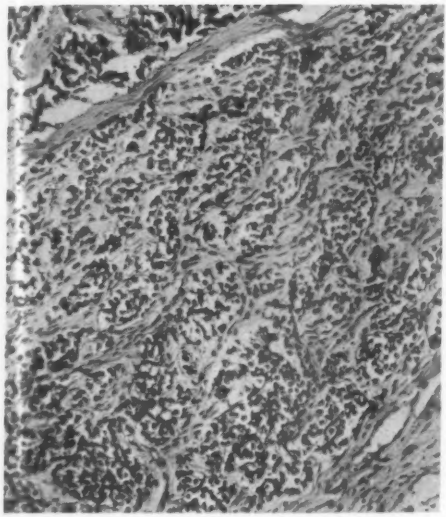

FIG. IX. Low power photomicrograph of a section of the tumour from Case 3 showing typical alveolar formation with more connective tissue than is usual. (x 75)

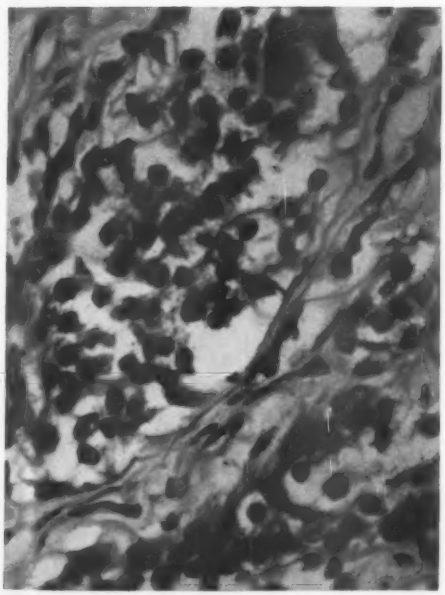

FIG. X. High power photomicrograph of a portion of the section of the tumour from Case 3 shown in Fig. IX. (x 350)

Autopsy showed an ante-mortem thrombosis of the left internal carotid artery from its origin to 2 cm. along the middle cerebral artery. The left cerebral hemisphere showed extensive softening and patchy haemorrhage which was most obvious in the region of the left basal ganglia. No evidence of any tumour was found.

The growth measured 6 cm. x 3 cm. x 2 cm. (Fig. VIII) and weighed 23 gm. It was roughly oval in shape and grooved on one side by the carotid vessels. It possessed a definite capsule and was smoothly lobulated. Histologically the tumour showed the characteristic structure (Figs. IX and X).

SOME GENERAL CONSIDERATIONS

Carotid body tumours have been known for many years but under a variety of names including perithelioma, endothelioma, angioma, phaeochromocytoma, sympathoblastoma, paraganglionoma and chromaffinoma. These synonyms are partly due to lack of appreciation of the special nature of the cells of the tumour and their relation to those of the carotid body but also to changes in the view regarding the structure and function of the organ.

Anatomy

The carotid body or glomus is situated in the crotch of the bifurcation of the common carotid artery. It is small, 5 mm. in its long axis, greyish to reddish in colour and may be of a uniform or lobulated appearance. It is invested by a capsule from which fibrous septa enter the gland dividing the masses of parenchymal cells into lobules. Vessels and nerves ramify in these septa. The blood supply is an ample one coming from the external carotid artery, while the nerve supply comes mainly from the superior cervical ganglion, the glossopharyngeal and the vagus nerves, together with twigs from the superior laryngeal and hypoglossal nerves (Tchibukmacher, 1938).

Embryologically it is connected with structures of the 3rd branchial arch (Boyd, 1937) whilst the aortic body of similar structure is related to structures of the 4th branchial arch.

Histologically the main feature of the normal carotid body is an extensive capillary network which is clearly defined by a thick endothelium. Nerve fibres are abundant, being intimately associated with both blood vessels and parenchymal cells. These are

large polyhedral epithelioid cells with a slightly granular cytoplasm. The cells contain darkly-staining, eccentric, round or oval nuclei, and are grouped in clusters which are related to the blood vessels. The cell clusters are separated by connective tissue septa which pass into the body from its capsule.

Physiology

The association of the carotid bodies with the branchial arteries is of special importance in fish which derive oxygen from water as it flows through the gills, and it seems probable that both the aortic and carotid bodies represent structures which, in water-breathing animals, control respiration (Krogh, 1941).

It is only in recent years that the carotid and the aortic bodies have been recognized as chemo-receptors responding to changes in the constitution of arterial blood. This conception is largely due to the work of Schmidt and Comroe (1940) and Dripps and Comroe (1944). Previously a variety of effects and functions had been attributed to the carotid body ranging from the production of osteomalacia in cats by destruction of the gland to an increase in blood pressure in rabbits following injection of an extract of the equine carotid body.

Confusion has long been caused by the presence of granules in some of the cells which have a weak affinity for chrome salts. Rationalization led to a grouping of the carotid body with the adrenal medulla. However, the chromaffin reaction, so-called, is non-specific and as Le Compte (1948) points out, various oxidizing agents other than chrome salts will give the reaction. He suggests that both carotid and aortic bodies should be classed as specialized chemo-receptors.

It is now well established that the chemo-receptors of the carotid and aortic bodies are stimulated by anoxic conditions where there is a subnormal oxygen tension, for example, narcotic poisoning, some types of clinical anaesthesia, anoxia associated with pathological changes in the lungs and high altitude flying. The reaction to an increase in carbon dioxide tension is negligible in physiological ranges and so is unimportant from the practical viewpoint; that due to change in pH and increase in blood temperature is still being investigated. In most cases, experimental bilateral denervation of the carotid bodies abolishes the stimulant effect of anoxia on respiration although, in a few cases, some response persists perhaps owing to unusually competent masses of chemo-receptors elsewhere.

The hyperpnoea of anoxaemia and narcotic poisoning is to an overwhelming degree reflex in origin, the component due to direct stimulation of the medullary centre by anoxia being negligible. Indeed the medulla is depressed by anoxia. The hyperpnoea due to an increased level of carbon dioxide and acid on the other hand is shown to be purely central in character.

In Case 2, Newton produced denervation *par excellence* of the carotid bodies, thus providing a therapeutic example of what is a difficult enough feat in the experimental animal. The investigations performed on this patient after excision of the tumours show that the response of the respiratory system to an increased percentage of carbon dioxide in the inspired air is that of a normal person. However, most subjects increase their respiration 25-35 per cent. when inhaling 10 per cent. oxygen. This patient showed only a very small response even when breathing 7 per cent oxygen. This result, while not proof (evidence of her reaction to anoxia pre-operatively was not available), is at least in conformity with the chemo-receptor hypothesis.

It has been shown by Gellhorn and Lambert (1939) that the stimulus required to produce a significant activation of the vasomotor system was in the neighbourhood of 7 per cent. oxygen in the inspired air. By denervation of the chemo-receptors, it has been shown in this patient as well as experimentally that the direct effect of anoxia on the circulatory system, like that on the medullary respiratory centre, is a depressant one. Thus the blood pressure in this patient, while breathing 7 per cent. oxygen, dropped from 140/90 to 120/85.

Three points remain: first, do the chemo-receptors play a part in the control of respiration in normal circumstances or do they function only in emergencies? The evidence adduced up to the present indicates

that a few of the chemo-receptors are sufficiently sensitive to be active under normal conditions but when a certain low threshold of oxygen partial-pressure has been reached, the mass of the receptors becomes involved. Secondly, how is the total effect of the chemo-receptors distributed between the aortic and carotid bodies and—if it should be proven a chemo-receptor (Guild, 1941)—the jugular body? Comroe (1939) found that, though there were wide individual variations in dogs, the carotid bodies will play the larger part in the production of the hyperpnoea of anoxaemia. Thirdly, although it has often been sought by every possible method, there is no evidence for the existence of an internal secretion from the carotid body. Assays for epinephrine have been repeatedly negative (Christie, 1933; Le Compte, 1948).

TUMOURS OF THE CAROTID BODY

These will now be considered from two aspects: first, their structure, both macroscopically and histologically and secondly, their resemblance to glomus tumours.

Clinically, carotid body tumours are slowly-growing, round or ovoid growths with a smooth lobulated exterior—an appearance which led to the term "potato growths" (Hutchinson, 1888). They occur equally in both sexes, are found most commonly in patients 30-60 years of age and are almost always unilateral. The size averages from 2-6 cm., but may be much more, in diameter. Reid (1920) reported one weighing 190 gm. whilst O'Shaughnessy described one 15 cm. across which, judging from its appearance, must have weighed considerably more.

The tumours have a firm, investing capsule. Their colour when cut is greyish to deep reddish-brown, the tissue being firm but somewhat elastic. They are very vascular, usually enveloping the bifurcation of the carotid arteries so that the last mentioned vessels lie in a groove or may even be enclosed within the tumour.

Histologically the tumours usually retain a very close resemblance to the normal carotid body consisting of typical polyhedral cells arranged approximately in alveoli. The cells, however, show more variation in size and shape than the normal gland and have hyperchromatic nuclei. The cell masses are separated by a variable amount of connective tissue which contains blood vessels and neurofibrils. The amount of connective tissue present determines the appearance of the tumour and they can be classified (Le Compte, 1948) as:

(1) the "usual" type in which there is a more or less faithful reproduction of the normal structure of the carotid body even, as will be shown later, to the extent of the nerve supply;

(2) the "adenomatous" type in which the parenchymal cells have a pronounced epithelial appearance and are arranged in sheets or strands. Here the reticulum is very scanty.

Le Compte (1948) refers to a third type or "angioma"-like tumour, in which the cells are spindle-shaped and closely related to capillaries. These groupings, however, represent only the predominant structure.

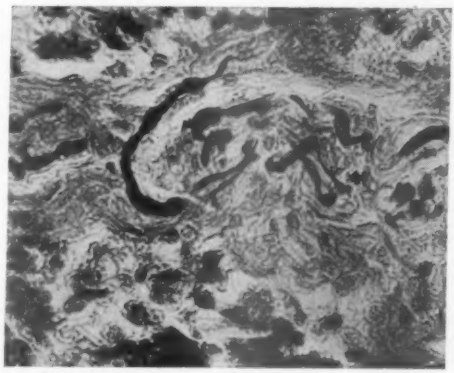

FIG. XI. Photomicrograph showing a typical appearance from a richly innervated area of a tumour. These nerves are in a fibrous septum and appear to show a cluster of nerve endings. An axon with a club-shaped ending can be seen (Case 3). (x 350)

Some authors (Chase, 1933) place emphasis on the occasional presence of groups of small hyperchromatic nuclei, the so-called sympathogonia cells. These cells were present in all tumours in this series but their arrangement and staining reactions, apart from the deeper-staining nucleus, were not different from that of the predominant cell present.

Occasional groups of small round cells were found, but such wandering cells are of common occurrence in tumours and hyperplasias.

The chromaffin reaction was present in a few cells in each of the tumours in this series, but was not at all comparable to that observed in the adrenal medulla. De Castro (1927) believed this chromaffin reaction to be due to the presence of lipoid granules while Hollinshead (1943) considers that the morphology of the granules in various circumstances suggests that they may actually be mitochondria.

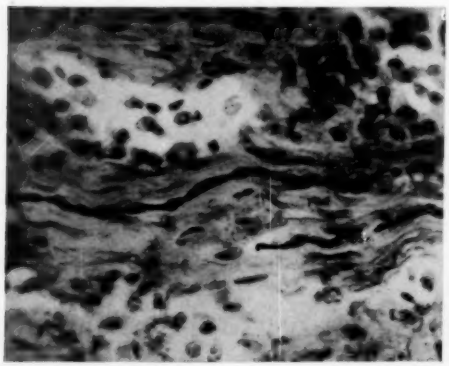

FIG. XII. Photomicrograph showing two axons, from a poorly-innervated area, running characteristically in the fibrous septum. Many nodal thickenings can be seen along the course of the axons (Case 3). (x 280)

The cytoplasm of the chief or polyhedral cells was commonly granular and they resembled very closely the granular polyhedral cells of the normal carotid body. Hollinshead (1945) has shown that the cells of the normal carotid body in the mouse under severe anoxia showed a degranulation and he interpreted this as showing that the cells are directly concerned with the initiation of chemo-receptor reflexes.

It has often been stated that nerve fibres are absent from these tumours (Bloom, 1943; Le Compte, 1948) or that only a few are present, while nerve endings, except perhaps in one case by Chase (1933), have not been demonstrated. It may be as Le Compte (1948) says that they have not been sought very often or, as Chase (1933) states, techniques are not sufficiently developed to differentiate reticular and nerve tissues sufficiently clearly but, whatever the reason in other cases, here, using a modification of a technique for formalin-fixed material (Willis, 1945), it has been shown unequivocably that both nerve fibres and nerve endings (Fig. XI) exist in these tumours. The nerve fibres were found irregularly distributed through the tumour, some areas showing a rich innervation whilst in other parts only occasional fibres were seen. The nerve fibrils ran especially in the connective tissue (Fig. XII) between the cell groups and occurred in the wall of blood vessels. Some fine fibrils were found among groups of parenchymal cells (Fig. XIII). The axons showed irregular thickenings along their course and terminated in broad endings.

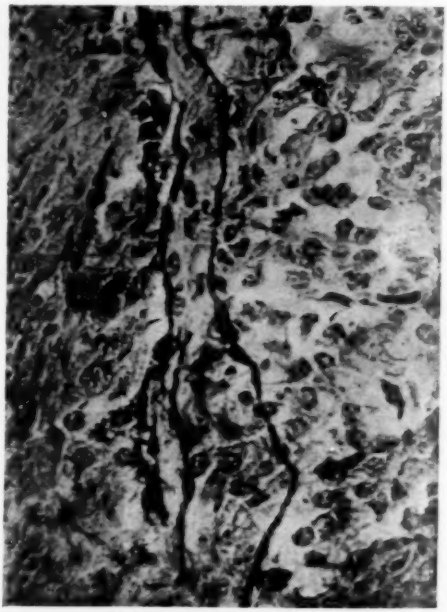

FIG. XIII. Photomicrograph showing neurofibrils traversing an area of parenchymal cells in a richly-innervated zone. Some irregularities can be seen along the course of the axons. (x 350)

Relation of Carotid Body to Glomus

Schumacher (1938) suggests that the cells of the carotid body are epithelioid muscle cells in the media of extremely tortuous arterio-venous anastomoses. Goormaghtigh and Pannier (1939) assert that the sole

blood supply to the carotid body's receptor tissue is through an arterio-venous anastomosis and that the chemo-receptor cells surround the venous segments of these vessels.

Masson (1937), however, states that " . . . *ces 'cellules épithélioides' n'ont pas dans tous la même signification*" and that, whilst in the glomus body they are modified muscle cells, in the carotid body they are glandular cells.

Glomus bodies have been recognized for many years as specialized arterio-venous anastomoses situated in the deeper layers of the corium of the skin commonly in the hand and foot. The anastomosis is opened up by heat (Grant and Bland, 1930) allowing blood to pass directly from artery to vein. The resulting increase in blood flow facilitates heat loss and these anastomoses probably account for the enormous changes in skin blood flow produced by wide changes in temperature.

The anastomotic vessel is S-shaped and the wall has an endothelial lining with two ill-defined muscle layers. Among the muscle cells are found groups of epithelioid cells while the anastomosis is surrounded by a collagen network with numerous nerve fibres.

Both the carotid and glomus bodies have important receptor functions, the first being concerned with respiratory exchange, the second with thermal exchange. They are structurally somewhat similar, both being vascular, liberally supplied with nerves and have similar reticulum frame-works.

The tumours to which both bodies give rise are remarkably similar in properties and behaviour ranging from a similar age and sex incidence to the same benignity of behaviour.

CLINICAL ASPECTS

There is usually a swelling of long standing and situated high in the neck. If the tumour be large it bulges the pharyngeal wall, when the patient complains of difficulty in swallowing. The patient occasionally complains of pain or throbbing in the neck and very occasionally of hoarseness.

It is remarkable, as many writers have commented, that so few cases of carotid sinus syndrome have been recorded in association with these tumours. This is additional evidence, were it required, for the completely separate identities of the carotid body and the carotid sinus. Gratiot (1943) suggests that the production of a carotid sinus syndrome in association with a tumour would require a hypersensitive sinus.

The diagnosis of carotid body tumour is difficult to make on clinical grounds alone, since aneurysm, metastatic malignancy, reticuloses, chronic lymphadenitis, "aberrant thyroid" tissue, and branchial cysts must all be considered.

Recently Idbohrn (1951) has reported three cases of carotid body tumour on which angiography was performed successfully,—two cases being investigated pre-operatively; Wright (1952) has also reported one case.

In all four patients the angiogram showed, at the site of the tumour, an extensive capillary network consisting of dilated tortuous and irregular capillaries. The external carotid artery was always displaced forwards and in two cases ended at the anterior border of the tumour.

Usually the diagnosis is impossible pre-operatively and was not made in any of the present small series. Furthermore Gordon-Taylor (1940) describes a case which clinically and at operation was thought to be a carotid body tumour while on section and histological examination it was found to be a neurofibroma.

Treatment is difficult in the experience of most writers, because of the frequent necessity (50 per cent. of cases) of ligating the common carotid artery and/or its branches. This is a serious matter since the operation carries a forbidding mortality and morbidity, the former being as high as 30 per cent. even in the most skilled hands.

Radiotherapy has been found to be almost uniformly unsuccessful. Bevan and McCarthy (1929) reported an apparently successful result but the patient was only followed for one year. Starr's (1944) case did not show any response whatsoever to efficient deep therapy while the writer knows of one case with a permanent radium implant which has produced no effect on the tumour in over 20 years except for the production of a radio-necrosis of the skin overlying the

tumour. One would actually not expect radiotherapy to affect such a slow-growing, well-encapsulated tumour.

Lahey and Warren (1947) consider that since "aberrant thyroid" tissue is always malignant and branchial cysts are easily removed and since some carotid body tumours can be demonstrated by exploration to be safely removable, all laterally located and discrete neck tumours should be explored.

Lewison and Weinberg (1950) recommended that the diagnosis of carotid body tumour should be kept in mind when dealing with tumours in the neck and that Peterson and Meeker's (1936) suggestion of gradual pre-operative compression of the carotid vessels should be practised. The last mentioned authors, however, found this technique only of use when pressure actually produced symptoms, since several deaths occurred in the absence of symptoms being produced by manual compression. A note of warning is necessary even where ligation of any carotid vessel is unnecessary. Case 3 is a salutary reminder that despite the carotid vessels all remaining intact and with an involuntary sympathectomy performed as well, carotid thrombosis, with resultant cerebral infarction, can occur.

DISCUSSION

There are two points worthy of special comment:

(1) Bilateral tumours

There have been seven histologically proven cases of bilateral carotid body tumours described by: Schmidt (1914); Rankin and Wellbrock (1931); Chase (1933); McNealy and Hedin (1939); Marangos (1939); MacComb (1948); Lewison and Weinberg (1950). Presumptive cases have been recorded by Lund (1916) and de Tarnowsky (1932). Doubtful cases are those of Middleton and Bierring (1897) and Gilford and Davis (1904). Middleton is usually given credit for recording the first bilateral case but as Gratiot (1943) points out, there was a bilateral occurrence of the tumours two months after removal of the right sided one. Death occurred one year later from cachexia. Grossly the tumour removed was said to resemble a carcinomatous metastasis. There were no microscopic sections and no autopsy report; and no case recorded since has grown with such rapidity.

Gilford and Davis (1904) reported a bilateral case the true nature of which is, however, doubtful.

Chase's (1933) patient died shortly after operation during which removal of both tumours was attempted and at autopsy both common carotid arteries were ligated. Lewison and Weinberg (1950) have described the most recent case. The patient was a 36 year old male with bilateral painless swellings present for 10 years in his neck. A right-sided exploratory operation was performed and a highly vascular tumour removed from the bifurcation of the carotid arteries without ligation of a major artery. Some four weeks later after carotid compression exercises the left tumour was successfully removed. Histological examination showed the typical structure of carotid body tumours. The writers state that they could not detect any difference in any of the known physiological functions of the carotid body. However, they give little account of the investigations done and no mention is made of the patient's reaction to anoxia.

Newton's patient, then, is the eighth histologically proven case but is almost certainly unique in that both tumours were successfully removed during a single stage operation. Rankin and Wellbrock's (1931) case may be comparable but they give no operative details.

The actual nature of the tumours is still debated and many authors (Reid, 1920; Chase, 1933; Lewison and Weinberg, 1950) think that they should be regarded as hyperplasias. In support of this suggestion is the very close resemblance between the structure of the tumour and that of the normal gland, the cells being very similar in both, and the demonstration in this paper of a comprehensive nerve innervation.

(2) Malignancy

There is a considerable discrepancy in the literature regarding the percentage of tumours found to be malignant, estimates

varying from 50 per cent. or more, to negligible proportions. The writer considers the figure of 50 per cent. to be completely out of proportion.

The criteria for malignancy applied by different authors vary considerably but definitely atypical cellular growth is rare. Mitotic figures are very rare though considerable variation in nuclear size with giant forms may occur. Case 1 (Fig. II) is an example where the histological appearance and clinical course do not agree: invasion of the adventitia of vessels can be seen in sections from the specimen yet neither recurrence nor metastasis was found at autopsy five years later.

Three cases of postulated visceral metastasis have been described. Gilford and Davis (1904) reported a case with metastases to the liver but there is doubt about the diagnosis and there is no illustration of the metastases. Goodof and Lischer (1943) recorded a case of carotid body tumour: at autopsy a small, poorly-demarcated nodule was found in the head of the pancreas. The section appears very fibrous and there is pancreatic tissue present in it.

Pendergrass and Kirsh (1947) have described a case of carotid body tumour with very widespread metastases to lungs, liver, vertebrae, femur, pelvis, ribs and sternum as well as the frontal bone. There is, however, no illustration of the primary growth but the illustration of the metastasis in the frontal bone would appear to closely resemble a carotid body tumour. Walton's (1947) first case is a good example of how a carotid body tumour can be mimicked by another growth. The primary in his case was a carcinoma of the pharynx which eventually fungated through the neck.

In the literature, although recurrence rates of up to 25 per cent. have been recorded, actual histological evidence of this recurrence is notably lacking. It would appear that, as in Case 1 of this paper, provided the tumour and capsule be completely removed no recurrence will be observed. Le Compte (1948) states that he could find only two cases of histologically verified spread to the lymph nodes and in one, the node had obviously been infiltrated by direct extension. Starr's (1944) case is presumably one of direct spread to the tonsil.

A case of interest is that of Kipkie (1947) who reported a patient in whom there was a right carotid body tumour present together with a tumour in the petrous portion of the left temporal bone. The last mentioned tumour had a similar structure to that of the carotid body tumour, but was known to be present some five years earlier. It is suggested that this tumour was probably derived from the recently recognized jugular body (Guild, 1941).

One must agree with Willis (1948) that "with few and doubtful exceptions tumours of the carotid body are benign, slowly growing, remaining sharply circumscribed and producing no metastases . . . Proof of the primary nature of a suspected (malignant) tumour will depend on careful necropsy to exclude the possible presence of a primary growth elsewhere."

CONCLUSIONS

(1) Carotid body tumours are not true neoplasms but are best regarded as hyperplasias.

(2) They are, for all practical purposes, benign in nature although occasionally, on histological examination, they may show some of the features of malignancy.

(3) The chromaffin reaction is weak and non-specific and the carotid body should not be grouped with the chromaffin system but as a specialized chemo-receptor.

(4) An extensive nerve innervation with club-shaped nerve endings can be demonstrated.

(5) A pre-operative diagnosis is often impossible but the tumour should be kept in mind when exploration of a mass in the neck is undertaken. Angiography may be of help in future cases.

(6) Radiotherapy is ineffective in treatment.

(7) Early surgery is the treatment of choice, but still carries a mortality of 30 per cent. Carotid thrombosis is still to be feared even though all carotid vessels be left intact.

(8) From study of the patient who had bilateral tumours successfully removed by Sir Alan Newton, the hypothesis that the carotid bodies are receptors, stimulated by anoxia, is supported.

(9) The glomus body and the carotid body have a number of features in common.

SUMMARY

Three patients who had carotid body tumours subjected to surgery are described, including a patient with bilateral tumours. In no case were any carotid vessels ligated, yet death occurred in a patient who had a unilateral tumour removed.

Post-operative investigations, performed on the patient who had had bilateral tumours, involving a variation in the percentage of oxygen in the inspired air, provide suggestive evidence in favour of the hypothesis that anoxaemia with a subnormal oxygen tension is the stimulus to the carotid bodies.

The histology of the tumours is examined and similarities to the glomus tumour noted. Their general structure indicates that they are hyperplasias; the tumour is extensively, if irregularly, innervated and many club-shaped nerve endings can be demonstrated. The "tumour" is therefore probably a functioning tissue.

Diagnosis and treatment are briefly discussed, early surgery being the treatment of choice, whilst angiography may help in diagnosis.

The literature of bilateral carotid bodies is briefly reviewed.

The percentage of malignant carotid body tumours is considered to be negligible.

ACKNOWLEDGEMENTS

I wish to offer my sincere thanks to Lady Newton for her kind permission to record the late Sir Alan Newton's case of bilateral tumours; to Mr. A. J. Trinca and Dr. J. E. Gillespie for the details of Case 1; and to Mr. H. A. Phillips for the details of Case 3.

I am grateful to Professor R. D. Wright, Professor of Physiology in the University of Melbourne, for providing the data obtained from the investigation of Sir Alan Newton's case, and to Dr. Andrew Brenan for his pathological report on this case and the photomicrographs of these specimens. The beautiful nerve preparations illustrated in this article are the work of Mr. A. G. Willis, M.Sc., of the Department of Zoology in the University of Melbourne.

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GIANT FIBROADENOMA OF THE BREAST

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MASSIVE tumours of the breast are rarely seen nowadays. This is because the public is becoming increasingly aware of the possible significance of breast tumours, and all tumours of the breast are therefore probably reported at an earlier stage than was the case in previous decades. Furthermore, in the neglected malignant cases, the tumour is usually fatal before the primary lesion has reached massive proportions.

Reports of giant tumours of the breast have appeared in the literature at infrequent intervals for more than a century, although there has been increasing attention to the subject in the last few years. The appearance of a young woman with a massive breast tumour in the Out-patient Department of a General Hospital created considerable interest, and it was apparent that the features of this tumour were not generally appreciated. It was decided to review the literature on this subject, and to examine the available records of the cases occurring in Melbourne in the last twenty-two years.

The lack of clear understanding of these growths is indicated by the observation that there are two views as to the nature of this tumour: one is that they are all benign, and the other that they are all malignant. In actual fact, as is known to be the case with many conditions, the real state of affairs is a compromise between the two views; most of the tumours are benign, but a few exhibit the features of malignancy.

The causes of massive tumours of the breast are as follows, in decreasing order of frequency:

(i) Diffuse hypertrophy;

(ii) Giant fibroadenoma;

(iii) Sarcoma;

(iv) "Colloid" carcinoma.

Diffuse hypertrophy is usually bilateral, being seen either at puberty or in the later years of the female reproductive period, and is due to an hormonal dysfunction.

Both sarcoma and "colloid" carcinoma of the breast, of gross size, are less common causes of massive tumours of the region than is giant fibroadenoma. However, when the total number of cases, both large and small, is considered, both sarcoma and "colloid" carcinoma of the breast are far more common. This indicates further that giant fibroadenoma of the breast is an uncommon condition.

The attempt to segregate the innocent tumours from the sarcomata, as has been attempted by some writers (McDonald and Harrington, 1950) is undesirable, since the two forms are related to each other, all gradations of rate of growth and involvement of surrounding tissues being found. Furthermore, the sole undeniable criterion of innocence or malignancy is the clinical outcome of the case. Attempts at histological differentiation are likely, in some cases, to fail.

So far, this tumour has been referred to solely as giant fibroadenoma of the breast. Two other names frequently applied to it in present times are *Cystosarcoma phyllodes* and Brodie's serocystic disease of the breast. *Cystosarcoma phyllodes* is not a good name because it emphasizes malignancy as an essential feature of these tumours. As was said earlier, only a few cases (about 12 per cent.), in the light of follow-up, behave as malignant tumours. Brodie's serocystic disease is a bad name because the tumours seen at present seldom exhibit large cysts, probably because they are now seen after a shorter history than those seen by earlier writers and hence show less evidence of degeneration. The association of Sir Benjamin Brodie's name with this tumour gives the impression that he was the first person to describe this tumour. This is not the case although, when he described it in 1846, he was the first to draw general attention to it and emphasize its cystic nature.

The common histological structure of the tumour tissue indicates that giant fibroadenoma of the breast (or sarcoma in the malignant cases), is a more satisfactory term.

HISTORICAL REVIEW

A study of early literature reveals a wide variety of names applied to this tumour. These early attempts at providing a satisfactory name for the condition appear to be based largely on the gross features. As will be seen later, these are varied and, as would be expected, this gave rise to a large number of cumbersome names many of which, in modern interpretation, would imply universal malignancy. Gradually, histological examinations were made and the number of names increased still further.

Some of the names seen in the early literature are as follows: cystic hydatids, glandular proliferous cysts, composite cystoid, cystosarcoma, cystic sarcoma, telangiectatic cystosarcoma, proliferous cystosarcoma, cystofibrosarcoma, intra-canalicular myxofibroma, intra-canalicular sarcoma, *cystosarcoma myxomatoides* and *cystosarcoma papillare.* An excellent account of the various names that have been employed, together with the writers who have suggested them, is given by Owens and Adams (1941). As can be seen from these names, the general opinion was that the tumour was a form of sarcoma with cystic change.

One of the earliest descriptions of this tumour was given in 1828 by Chelius, who wrote as follows: "The sarcomatous or steatomatous degeneration of the mammary gland is one of the most benignant diseases to which that organ is subject, as it is with great impropriety that many have spoken of it as carcinoma mammae hydatides. It is characterised by the large size and great prominence of the tumour. . . . The greatest diameter is not at its base, but at a point some distance from the walls of the chest . . . but other circumstances which serve still further to distinguish it, are its different consistence at different parts . . .; its mobility in all directions, notwithstanding the great size it attains; . . . the absence of swelling of the axillary glands. Although this tumour is inconvenient to the patient from its size and painful from its dragging at the surrounding parts, yet it does not affect the health."

Ten years later, in 1838, Johannes Müller gave a more accurate and detailed description of the tumour and he called it *cystosarcoma phyllodes.*

Lee and Pack, in 1931, published an analysis of all cases reported in the literature up to that time, listing 111 cases since 1828, with the various names applied to them. It is interesting to note that theirs is the only article (excepting the originals) referring to cases occurring in the male breast. They record three cases which, as far as can be determined, can quite legitimately be included in a discussion on this subject. Of this large series, 91 cases were "followed up" and in only six cases was there any recurrence of the tumour after removal.

Since the review of Lee and Pack in 1931, a number of cases has been reported in the literature. In 1941, Owens and Adams listed a further 10 cases and in 1950, McDonald and Harrington presented 13 cases of their own and recorded a further 11 cases from the literature, 8 of which had apparently been overlooked by Owens and Adams (1941). McDonald and Harrington (1950) excluded two cases from their series because they were malignant, but this is not justifiable, as it has been mentioned previously that this may be one of the features of the condition. It is also interesting to note that McDonald and Harrington (1950) report 4 bilateral examples amongst their cases; and of the cases overlooked by Owens and Adams (1941), 3 were bilateral.

More recently, Treeves and Sunderland (1951) have reviewed a series of 77 cases at the Memorial Hospital, New York, from January, 1930, to July, 1949. Of these cases, 41 were classified as benign, 18 as borderline and 18 as definitely malignant. It is noteworthy that the average age of the malignant group was at least five years younger than the average age of either the benign or borderline groups. Of their series, only eight patients died with evidence of recurrence and/or metastases and another two cases were still alive with recurrences present. As their cases have been followed for at least one year, and in most cases longer, it appears that all their borderline cases and some of their cases regarded, on histological grounds, as malignant were, in

actual fact, benign. This is further evidence that the prognosis of the tumour cannot always be predicted with certainty from the histological picture.

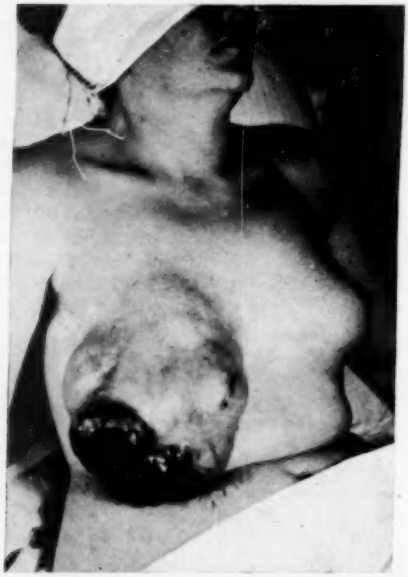

FIG. I. Photograph of patient (Case 1) showing the irregularly enlarged and lobulated right breast, with areas of ulceration. Its size is indicated by the comparison with the left breast. See Figs. II and III.

The cases used in the present series have been selected from the records of three General Hospitals in Melbourne during the past twenty-two years, and to these cases have been added five private cases (Cases 3, 4, 6, 8 and 9). This series does not represent all cases that have occurred in this period, for the varying nomenclature makes it difficult to trace every case, and when there has been any doubt at all, the case has been excluded. McDonald and Harrington (1950) state that, to be included in a series of giant tumours of the breast, the tumour must occupy at least four-fifths of the breast and must weigh at least one pound. This is a good working basis, but would exclude some tumours which exhibit all the other characteristics of a giant fibroadenoma of the breast, but which are prevented from coming to a significant size because they are observed and treated at an early stage as, for example, Case 7 of this series.

CASE HISTORIES

Case 1

A single woman, aged 26 years, had noticed a lump in her right breast for eighteen months. The lump had increased in size slowly for sixteen months and rapidly during the next two months. There was no relation between changes in the size of the tumour and the patient's menstrual history. Her general health was good. About six months earlier, her sister, aged 40 years, had had a radical mastectomy performed for carcinoma of the breast.

Examination showed a grossly enlarged and lobulated breast with three areas of skin ulceration (Fig. I). There were numerous dilated veins running over the tumour. The mass was not fixed to deeper structures and axillary lymph nodes were not palpable.

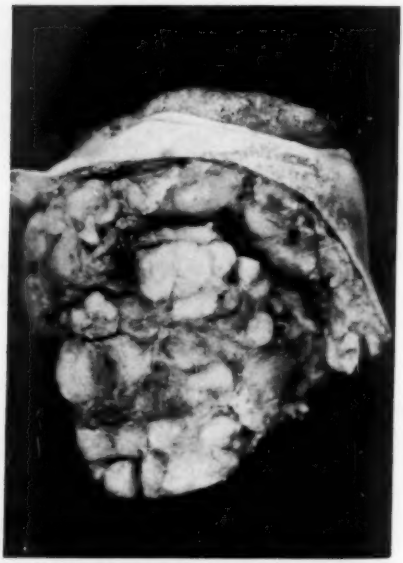

FIG. II. Photograph of the under-surface of the tumour after removal (Case 1). The lobulated character of the tumour is shown. It measured 6¾″ x 6¼″ x 4¼″. See Figs. I and III.

Simple mastectomy was performed and convalescence was uneventful. The tumour removed weighed 3 pounds and measured 6¾ inches by 6¼ inches by 4¼ inches. The tumour was grossly lobulated (Fig. II) and microscopically was seen to be a mixed pattern of intra-canalicular and peri-canalicular fibroadenoma, with a moderately cellular connective tissue (Fig. III).

The patient is alive and well, with no recurrence six months after operation.

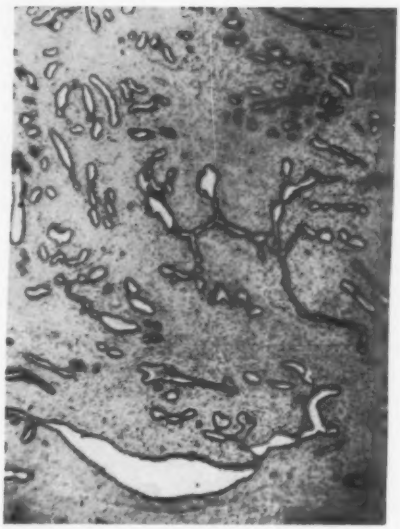

FIG. III. Photomicrograph of portion of the tumour removed from Case 1 (see Figs. I and II), showing the moderately cellular connective tissue and the epithelial tissue arranged both as long clefts and as alveoli (x 25). (Haematoxylin and eosin).

Case 2

A married woman, aged 22 years, had noticed a lump in her right breast for four years. There was no alteration in size until she was two months pregnant, when the lump began to enlarge. Local excision was performed, but apparently inadequately, for the lump recurred and grew rapidly. Ten months after this excision, examination revealed a mass in the right breast 6 inches in diameter and 3 inches deep, with a superficial ulcer 3 inches by 2 inches. The edges were raised, giving an appearance of fungation. A diagnosis of carcinoma of the breast was made and a course of radiotherapy was given, followed by radical mastectomy. The microscopic picture, after radiation, was one of diffuse myxomatous connective tissue with no epithelial tissue and no evidence of malignancy.

This patient was alive and well with no evidence of recurrence twelve years after operation. She has not been traced in the next ten years. Originally this case was considered to be malignant, but the subsequent history of the patient indicates that there was no recurrence or spread.

Case 3

A married woman, aged 45 years, received a blow on her left breast and two months later, she noticed a lump in the same breast. The size of the lump increased rapidly and five months later, radical mastectomy was performed.

The tumour weighed 3 pounds and the maximum diameter was 5 inches. Histologically the tumour showed the structure of the intra-canalicular type of fibroadenoma, with quite a cellular connective tissue.

The patient is alive and well fifteen years after operation, with no evidence of recurrence.

Case 4

A married woman, aged 38 years, had noticed a small nodule in her left breast fifteen months previously. It appeared just before a confinement. The baby was breast-fed for ten and one half months and the patient then noticed that her left breast was considerably enlarged.

Simple mastectomy was performed and convalescence was uneventful. The tumour removed occupied two-thirds of the breast and was about 6 inches in diameter. Microscopically, the tumour was seen to resemble the intracanalicular type of fibroadenoma with a cellular connective tissue and several areas of myxomatous degeneration.

The patient is alive and well 11 years after operation with no recurrence of the tumour.

Case 5

A single woman, aged 55 years, had noticed a lump the size of a hen's egg in her left breast for five years. Two months prior to being seen, rapid enlargement of the lump began and she became progressively weaker. The left breast measured 15 inches by 9 inches and was irregular and covered with small dilated veins. The tumour was not attached to deeper structures.

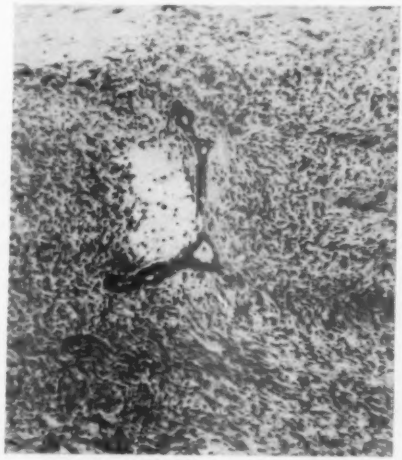

FIG. IV. Photomicrograph of portion of the tumour removed from Case 5, showing the extremely cellular connective tissue, with only a small cleft lined by epithelial tissue (x 75) (Haematoxylin and eosin).

Simple mastectomy was performed and the tumour weighed approximately 17 pounds. Histologically, the tumour was seen to consist mainly of a very cellular connective tissue with little epithelial tissue present (Fig. IV).

There was a recurrence in the scar soon after operation and this was excised one month after the first operation. Histologically, the recurrence consisted entirely of a very cellular fibrous connective tissue with numerous mitotic figures (Fig. V).

There was a further recurrence, which was excised three months after the first operation. The patient died ten months after her first operation with evidence of pulmonary metastases.

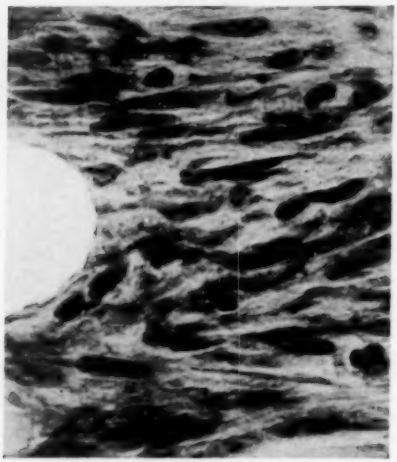

FIG. V. Photomicrograph of a section of the first recurrence of the tumour in Case 5, showing the very cellular stromal structure without epithelial tissue. On the left of the field is a large fat-cell. Also, some mitotic figures can be seen (x 700) (Haematoxylin and eosin).

Case 6

A married woman, about 39 years of age, had noticed a lump in her left breast for five years. In the six months prior to seeking medical attention, the tumour grew rapidly and radical mastectomy was then performed.

The tumour removed at operation was 4 inches in diameter. Microscopically, the tumour consisted of roughly equal proportions of intracanalicular and pericanalicular patterns, with a moderately cellular fibrous connective tissue.

The patient is still alive with no evidence of recurrence ten years after operation.

Case 7

A single woman, aged 63 years, had noticed a lump in her right breast for one month. Examination revealed both breasts enlarged and pendulous, but in the upper and outer quadrant of the right breast was a freely mobile lump measuring 2 inches by 1 inch. Local excision was performed and the tumour had numerous papillary processes and an almost gelatinous appearance.

Microscopically, the tumour was seen to have a very densely cellular connective tissue and very little epithelial tissue.

The patient is alive and well with no recurrence one year after operation.

This case is included in the series in spite of the small size of the tumour, because the appearance, both macroscopically and microscopically, resembled that of other members of the series, and because it seemed apparent from its rate of growth that, had it not been removed, it would rapidly have come to the large size of other specimens described here.

Case 8

A single woman, aged 48 years, stated that for two months her right breast had been larger than the left. This enlargement was due to the presence of a tumour which was later found to measure 7 inches by 5 inches by 5 inches. There were numerous dilated veins visible under the skin of the right breast and the tumour was not fixed to skin or deeper structures.

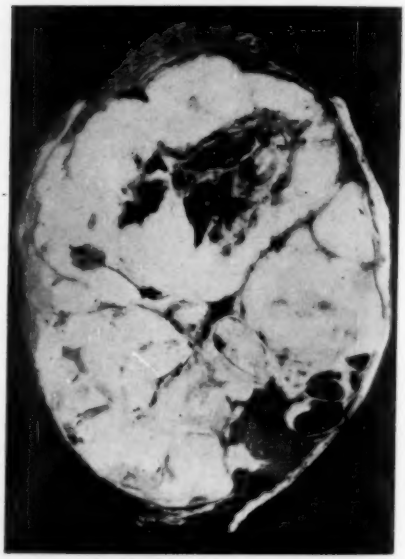

FIG. VI. Photograph of a cross-section of the tumour removed from Case 8, showing its homogeneous structure with several small cystic areas. It measured 7" x 5" x 5". Histologically it was an actively growing fibroadenoma in which the stroma predominated.

Simple mastectomy was performed and convalescence was uneventful. The cut surface of the tumour showed a fairly homogeneous tumour with several cystic areas (Fig. VI). Histologically, the tumour was seen to have a cellular connective tissue with only small amounts of epithelial tissue.

The patient is alive and well with no recurrence four years after operation.

Case 9

A widow, aged 53 years, had had a gradually increasing swelling of the right breast for nine years. For the two years prior to being seen, she had been unable to leave her house because of the size of the tumour (Fig. VII). After an attack of influenza, she was no longer able to carry the tumour and sought medical attention. Further questioning revealed that her husband had died previously of carcinoma of the stomach.

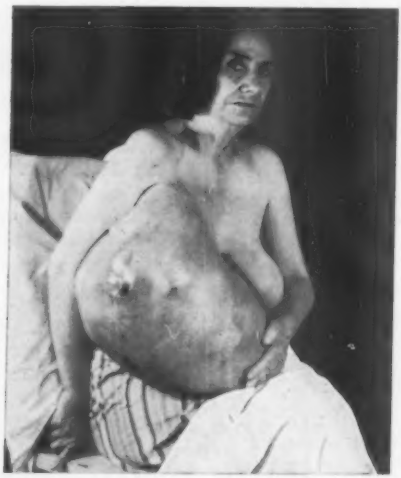

FIG. VII. Photograph of the patient (Case 9) showing the enormously enlarged right breast. It was irregularly lobulated and there were a few small points of superficial ulceration of the skin. It required a special support when the patient was ambulatory. When removed it weighed 27¼ pounds. See Figs. VIII, IX and X.

Simple mastectomy was performed and the tumour removed weighed 27¼ pounds and measured 15 inches by 12 inches by 12 inches. Two years later there was a local recurrence of the tumour. This was excised but the patient died suddenly five weeks later. Post-mortem examination revealed a pulmonary embolus, but no evidence of local recurrence or distant metastases was found. The recurrence was found to weigh 7½ pounds.

Cross-section of the original growth showed a relatively homogeneous fibrous type of tissue with some haemorrhagic areas and, also, an area with a "cauliflower" appearance (Fig. VIII).

Histologically, the main portion of the tumour was composed of fibrous connective tissue with little epithelial tissue. The "cauliflower" portion showed alveoli resembling the ducts of normal breast tissue lying in a cellular fibrous connective tissue (Figs. IX and X). The metastasis showed the appearance of a fibrosarcoma, being cellular

FIG. VIII. Photograph of a cross-section of the tumour removed from Case 9, showing two different areas. The bulk of the tumour is fairly homogeneous, with several haemorrhagic areas, while the smaller portion shows a "cauliflower" appearance. It measured 15″ x 12″ x 12″. See Figs. VII, IX and X.

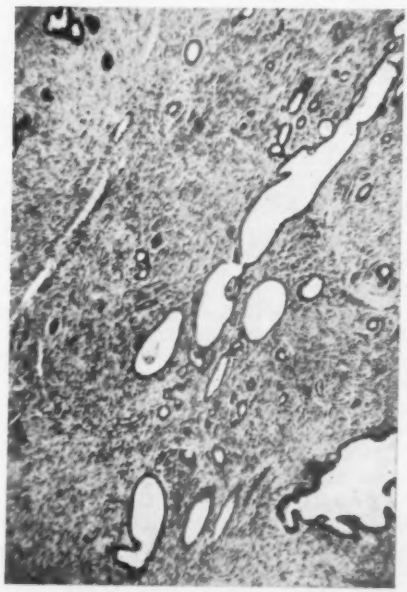

FIG. IX. Photomicrograph of portion of the main part of the tumour removed from Case 9, showing a very cellular connective tissue, with relatively little epithelial tissue (as compared with Case 1, Fig. III). (x 25) (Haematoxylin and eosin).

with vesicular nuclei and mitotic figures, and no epithelial tissue was demonstrated. This was the same appearance as in the metastasis of Case 5.

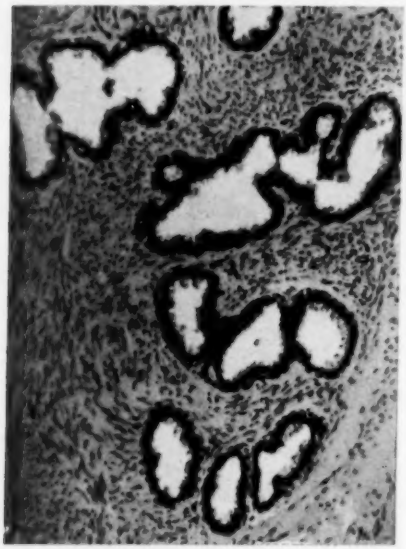

FIG. X. Photomicrograph of the "cauliflower" portion of the tumour from Case 9, showing the very cellular fibrous connective tissue and the epithelial tissue arranged as alveoli — the cells resembling those of the ducts of normal breast tissue. The general form is that of an inter-canalicular fibroadenoma. (Other parts are of the intra-canalicular type) (x 75) (Haematoxylin and eosin).

DISCUSSION

Giant fibroadenoma of the breast is an uncommon condition and, when encountered, will attract attention because of the arresting feature of the association of large size with, usually, clinical innocence. In the period 1946 to 1951 inclusive, only 4 cases were encountered amongst the tumours studied during an investigation into this condition. During the same period, 1,372 new cases of carcinoma of the breast were recorded by the Anti-Cancer Council of Victoria. These figures are both taken from almost the same general population. The list of carcinomata of the breast also includes 10 cases occurring in males, so that carcinoma of the male breast might be said to be about two to three times as common as giant fibroadenoma of the breast.

This uncommon tumour is practically confined to the female breast, although Lee and Pack (1931) list 3 apparently authentic cases occurring in males. The majority of cases is seen in women in the fifth and sixth decades and the tumour is unilateral in most cases, affecting right and left sides equally. McDonald and Harrington (1950) cite 3 bilateral cases occurring in girls near puberty, indicating a somewhat earlier age incidence for bilateral cases. However, in these cases, there is some reason (inadequate documentation) for doubting the diagnosis, as they may have been merely cases of diffuse hypertrophy of the breast.

Giant fibroadenoma of the breast is seen in both single and married women in almost equal proportions and parity seems to have little effect on the incidence of the tumour. Pregnancy definitely appears to be an exciting factor in a small proportion of cases, particularly when the patient has had a fibroadenoma in her breast for some time. Trauma seems to play the same minor role in the aetiology of these tumours as it does in most other breast tumours.

There are two different types of growth rate in these tumours: either the tumour enlarges steadily and more or less uniformly, or more commonly, the tumour remains stationary and then suddenly rapidly increases in size. The two different types of growth rate do not show any corresponding difference in microscopic appearances, and there is no apparent universal precipitating factor in the cases which enlarge suddenly after a period of quiescence. Several explanations have been offered, but none has been completely satisfactory. It is certainly not due to the onset of malignant change.

The tumour is characteristically large and lobulated and its cut surface may show several different features. The majority of tumours show a homogeneous fibrous appearance, whilst others show numerous intracystic papillary processes, frequently packed so tightly that once they have been displaced, they cannot be replaced; this second type of appearance is often described as being like either a cauliflower or an onion. Cysts are not seen so frequently these days, possibly because the tumours encountered are younger than those seen by the earlier writers. Where the tumour is composed of fibrous tissue, in older tumours or rapidly growing tumours there may be degeneration of the connective tissue with cyst formation.

and, in some cases, haemorrhages. The tumours with numerous papillary processes frequently possess cysts, but the cysts are usually only small. Strictly speaking, it is only when large cystic areas are present that the term Brodie's serocystic disease should be used; however, it is commonly used in a loose manner.

The size of the tumour varies considerably depending on several factors, but mainly, of course, on the age of the tumour. One of the largest tumours was that reported by McKenzie in 1935. The tumour weighed 35 pounds and had been present for only two years. The actual size of the tumour is of little consequence as far as malignancy is concerned, but as a phenomenon adds greatly to the interest of the case.

Histologically there is quite considerable variation in the nature of the tumour. The variation affects both the stroma and the epithelial portion of the tissue. The epithelial portion may be represented merely by a few long clefts of epithelial cells, as is seen characteristically in the intra-canalicular type of fibroadenoma, or there may be added to this varying amounts of epithelial tissue arranged as alveoli. The variation in the connective tissue portion is mainly in the cell density. On the one hand there may be very few connective tissue cells present, or on the other these may be present in large numbers. Not only are there all grades between the two extremes but also the variations in the two different kinds of tissue in the tumour are independent of each other; so that there are numerous possible appearances.

Malignant change is not a common feature in these tumours. The actual observation of the incidence of malignancy shows considerable variation in published papers, but a survey of the literature indicates that the figure most universally accepted is about 12 per cent. The order of malignancy in most cases is not as high as is found in other sarcomata. Usually, there is local recurrence of the tumour; distant metastases usually appear late. In some cases, it may be difficult to tell microscopically if the tumour is benign or malignant and, in these, the only certain way to estimate this is to excise the tumour and await the results of treatment. Should there be a recurrence, then usually the tumour can safely be designated as malignant. The first one or two recurrences are usually local and the common history is that it is not until one or more local recurrences have been excised that distant metastases appear.

When malignant change does occur, it is apparent in the connective tissue portion of the tumour, so that the malignant cases are sarcomata. This is borne out by the observation that when there are recurrences microscopic examination may not reveal any epithelial tissue at all but only a connective tissue which is usually very cellular with numerous mitotic figures.

The tumour itself produces few symptoms. In the smaller cases, the patient merely notices a lump in the breast, whilst in the larger cases the patient may complain of deformity, disability from the weight of the growth, or pain from the dragging at the chest wall by the tumour. In a small percentage of cases, ulceration of the skin may occur with fungation of the tumour substance and a serosanguinous discharge. When secondary infection occurs, the discharge becomes foul. Ulceration of the skin is usually confined to the larger or more rapidly growing tumours and is due to pressure necrosis of the skin. Nipple discharge and retraction are almost invariably absent, the nipple being normal or flattened by the expanding tumour. The general health of the patient remains unaffected unless there is secondary infection of an ulcerated area or there are invasion of deeper tissues and metastases.

Examination of the patient shows a large irregular tumour, in most cases occupying almost the whole of the breast. Usually there are areas of different consistence, some areas being quite firm, whilst others are quite soft or, in some cases, even fluctuant. The growth is globular in form, the main diameter of the tumour being not at its base but at some distance from the chest wall. This is because the tumour does not attach itself to the chest wall (except when malignant) but, because of its size and weight, it draws the breast outward forming a relative pedicle of soft tissue. Fixation to the skin does not occur unless, when the growth becomes contiguous, there is ulceration and infection of the skin; and

fixation to deeper structures is only found in some malignant cases. When the tumours are relatively small, occupying a small portion of the breast, they are freely mobile. Dilated subcutaneous veins are frequently seen coursing over the surface of the tumour. Enlargement of the axillary lymph nodes is the exception rather than the rule and, when present (provided that other unrelated causes have been excluded), is due to secondary infection of an ulcerated area. As the malignant types of this tumour are sarcomata, they spread by local infiltration or via the bloodstream, not via the lymphatics, so that lymph node enlargement does not indicate malignancy of the tumour.

The points in favour of a diagnosis of giant fibroadenoma of the breast are: a large irregular breast tumour, usually present for a considerable period of time, not fixed to skin or deeper structures and with no enlarged (hard) axillary lymph nodes, in a healthy woman, usually in the fifth decade of life. Conditions which may cause confusion are diffuse hypertrophy of the breast, "colloid" carcinoma of the breast and large lipoma of the breast.

Diffuse hypertrophy of the breast is usually bilateral and the breasts are evenly enlarged, retaining a more or less normal but enlarged contour. Also, there is no

TABLE 1

TABULAR PRESENTATION OF THE PRINCIPAL FEATURES OF THE CASES DESCRIBED

Seven of the cases were innocent in type, their average age (at times of treatment) was 42 years; the average age of the malignant cases was 54 years. Most of the cases had a long history but the stage of rapid growth (immediately prior to treatment) was short. The histological appearances varied, though stromal proliferation predominated. Local excision was performed in a majority of cases.

Case	Age	Marital State	Side	Period of Quiescence	Period of rapid Growth	Size	Histological Features	Treatment	End Result
1	26	Single	Right	16 months	2 months	6½″ x 6½″ x 4½″ 3 pounds	Predominately epithelial	Simple mastectomy	Alive and no recurrence 6 months later.
2	22	Married	Right	48 months	10 months	6″ x 3″	Predominately loose connective tissue	Radical mastectomy after radiotherapy	Alive and no recurrence 12 years later. Not traced for next 10 years
3	45	Married	Left	?	5 months	3 pounds	Predominately cellular connective tissue	Radical mastectomy	Alive and no recurrence 15 years later
4	38	Married	Left	10 months	5 months	6 inches in diameter	Predominately cellular connective tissue	Simple mastectomy	Alive and no recurrence 11 years later
5	55	Single	Left	5 years	2 months	15″ x 9″ 17 pounds	Predominately very cellular connective tissue	Simple mastectomy	Local recurrences one and four months later. Died 10 months after first operation with pulmonary metastases
6	39	Married	Left	12 months	6 months	4 inches in diameter	Slightly more epithelial than connective tissue	Simple mastectomy	Alive and no recurrence 10 years later
7	63	Single	Right	—	1 month	2″ x 1″	Predominately very cellular connective tissue	Local excision	Alive and no recurrence one year later
8	48	Single	Right	?	?	7″ x 5″ x 5″	Predominately cellular connective tissue	Simple mastectomy	Alive and no recurrence 4 years later
9	53	Widow	Right	9 years	—	15″ x 12″ x 12″ 27½ pounds	Predominately cellular connective tissue	Simple mastectomy	Local recurrence 18 months later. Died of pulmonary embolism 2 years after first operation

actual tumour in diffuse hypertrophy, the breast being of uniform consistence and softer than the tumour in giant fibroadenoma. "Colloid" carcinoma usually has a shorter history, is fixed to skin or deeper structures and causes enlargement of the axillary lymph nodes. The tumour is also of fairly uniform consistence. Large lipomata of the breast are extremely rare and when present, the tumour is very soft and often not readily distinguishable from the rest of the breast. In all these cases, should there be any doubt after clinical examination, then the histological picture will clinch the diagnosis.

The treatment of giant fibroadenoma of the breast is local excision whether the tumour is benign or malignant. Radical removal of the breast with removal of the lymph nodes is both unnecessary and indicative of ignorance of the true nature of the condition. That the treatment is local excision for all cases may seem debatable. However, if the tumour is innocent, local excision is sufficient and if it is malignant, then radical removal will not improve the prognosis. In either case, a mutilating operation is not necessary. As mentioned earlier, in many cases it is impossible to ascertain whether the tumour is innocent or malignant until it has been removed and the subsequent progress noted for some time. Some of the breast sarcomata, described in the literature, which were cured by radical mastectomy, were almost certainly examples of giant fibroadenoma.

The name Bloodgood is usually associated with breast lesions, and it is rather fitting that a statement he made in reference to bone sarcomata should apply equally well to this breast lesion. He stated that whilst local excision would cure some bone sarcomata, nothing at all would cure the others.

The recurrence rate after local excision is quite low and any recurrence is usually in the scar. In this series, only two cases developed recurrences, while in the series of Lee and Pack (1931) only 6 cases of the 91 traced developed recurrences. It is important to note that local recurrence does not always mean that the tumour is malignant; particularly in the case of large tumours local recurrences may be the result of incomplete removal of the growth.

Thus the prognosis in the benign variety is good, but in the malignant variety the best that can be hoped for is a limited period of survival after the patient first reports for treatment.

SUMMARY

A series of 9 cases of giant fibroadenoma of the breast has been presented to illustrate the features of a somewhat uncommon but none the less interesting condition. There is a typical clinical picture and, if one is not completely overawed by the size and appearance of the tumour on first inspection, in the majority of cases the patient can be treated quite effectively by relatively simple means. However, it should be remembered that there is a small proportion of these tumours which is malignant.

ACKNOWLEDGEMENTS

I would like to offer my sincere thanks to Mr. Henry Searby, Mr. Balcombe Quick, Mr. N. M. Harry, Dr. A. M. Hill and Dr. Ian Pender for their encouragement by provision of clinical notes of patients. Also, I would thank the Medical Staffs of the Royal Melbourne, Women's and Prince Henry's Hospitals for permission to use cases from their records.

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FIG. I. The title-page of the 1545 edition.

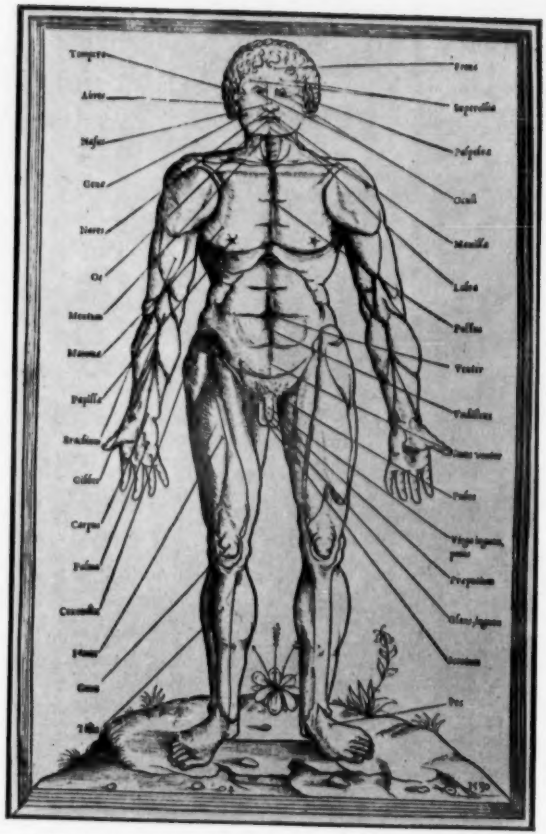

FIG. II. The earliest dated plate in Estienne's book. It it signed with Jollat's monogram and shows the surface anatomy.

The College Library

THE *DE DISSECTIONE* OF CHARLES ESTIENNE

By K. F. Russell

Department of Anatomy, University of Melbourne

IN 1545 Charles Estienne, with the assistance of Etienne Riviere, published in Paris a text book of anatomy with the title *De dissectione partium corporis humani* which gives us a clear picture of the state of anatomical knowledge in the immediate pre-Vesalian period. The author, also known by the latinized version of his name, Carolus Stephanus, was a member of a well known family of publishers in Paris and author of a number of scientific and medical books. He was born about 1500, worked for some time in his brother's printing house, received the Degree of Doctor of Medicine of Paris in 1542 and died in 1564.

He had been working on his book for many years before it was published for one of the plates is dated 1530 and he tells us in his preface, which he addressed to his students, that the work was completed and actually in print up to the middle of the third book in 1539, when, because of a dispute that had arisen (*ob enatam controversiam*), the whole work was suppressed. The dispute, which was long drawn out, was between Estienne and Riviere the Paris surgeon who had helped him with the dissections and also with some of the illustrations for his monogram appears on one of the skeletal plates in the book.

During the dispute Estienne experienced trouble in guarding the parts of the book set up in print for he tells us in the preface that portions of the book and some of the plates were taken to Germany and we now know that they were used by two printers, Balthasar Beck and Christian Egenolph, without Estienne's knowledge or approval. He had further trouble with plagiarists for, in 1557 and again in 1575, Jacques Kerver published a set of the Estienne woodcuts in Paris entirely without acknowledgment.

To prepare the plates it is apparent that Estienne and Riviere performed a number of dissections for he tells of the debt he owes the latter for his zeal in the matter of dissection and towards the end of the book there are a large number of small woodcuts of the separate muscles of the body which show evidence of detailed knowledge.

The book was at once popular for, apart from the *Fabrica* of Vesalius, it was the most richly illustrated work that had appeared and the Latin edition of 1545 was followed by a French translation the next year.

There are a total of 62 full-page plates (including 6 which are duplicates) and 101 small woodcuts of the orbit, individual muscles and the spinal cord. Of the large plates 6 are signed (Plates 1, 13, 14, 15, 16 and 17) and 4 of these are dated as well as signed (Plates 14, 15, 16 and 17) the dates being 1530, 1531 and 1532. Four of the plates carry the signature of François Jollat or his monogram, one carries the monogram of Riviere and one the cross of Lorraine which also appears on all of the Jollat plates. In the case of the rest of the plates there is no indication of the responsible artist.

With the exception of the signed skeletal plate the other signed plates are of an earlier period and differ in character to the rest. They are simple plates showing surface anatomy and the superficial muscles. The one dated 1530 is very similar in pose and appearance to the early sixteenth century woodcuts of the zodiac man that appeared in a number of books. Nearly all the other plates are stiff and unreal with a maximum of useless background and a minimum of anatomical detail; indeed, in some, it is not at first sight clear which anatomical

point is being shown. The plates showing female anatomy are better drawn and more pleasantly posed than the others. Many of the plates show an interesting technique in preparation; the anatomical detail being on small blocks inset into the larger woodcut which shows the outline of the figure and background. This economy of woodcutting would suggest that the larger figures had been made for use in another book but Estienne did not repeat these figures in his book by altering the inset nor has another book using these figures come to light.

The small woodcuts in the book show much better anatomical detail than do the large ones. When the French edition came out in 1546 Estienne added two skeletal plates which did not appear in the earlier edition.

The text of book shows a better anatomical knowledge than is displayed in the plates and although the author leans rather heavily on the teachings of Galen there is evidence of original work. In spite of errors in the book and the rather unpleasing plates, Estienne's work fills an important position in the history of anatomy and must be examined by all who seek a picture of pre-Vesalian anatomy.

The copy in the possession of the College is a particularly fine one.

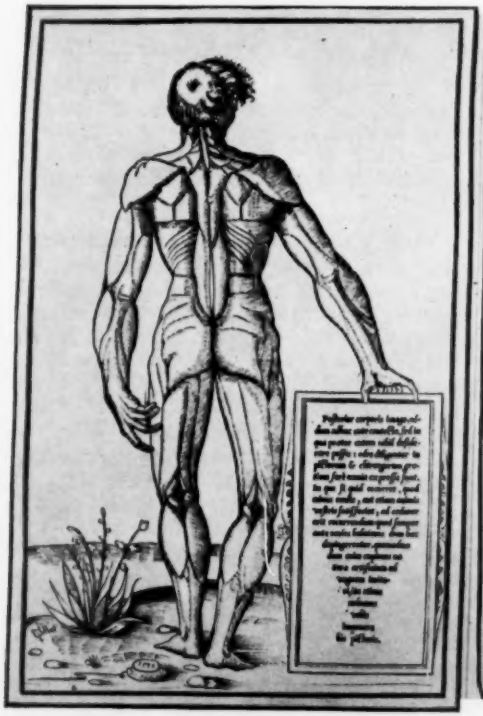

FIG. III. Another signed and dated plate showing the superficial muscles from the back.

FIG. IV. One of the visceral plates. The use of the small inset in the large woodcut block is well shown.

EXTRUSION OF INTACT HYDATID CYST

By J. T. Hueston

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INTRA-PERITONEAL rupture of a hydatid cyst of the liver is of importance not only as an abdominal catastrophe, often with a fatal termination, but also as an episode in the life of the parasite. The effects will depend both upon the magnitude of the leakage and on the state of the cyst which has ruptured. It is necessary, when considering the problem of intra-peritoneal rupture of hydatid cysts of the liver, to keep in mind the possibility of the rupture involving only the adventitia and thus of the cyst being extruded intact.

The occurrence of this uncommon phenomenon has been recognized for many years. One of the earliest examples recorded in the literature is that of Allen (1882), and other cases have been reported and discussed by Laveran (1892), Guibal (1905), MacCormick (1907), Dévé (1911), Cranwell (1912) and Orihuela (1935). It is felt that such an uncommon event is of sufficient interest to warrant reporting a new case in this paper.

Case Report

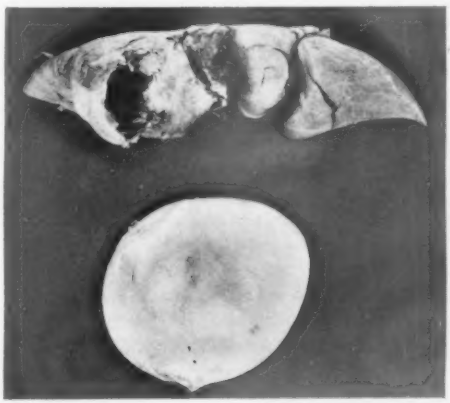
The patient (J.N.), a male, aged 79 years, was admitted to the Royal Melbourne Hospital on 30th January, 1950, in a state of congestive cardiac failure with a moderate degree of hypertension (160/100 mm. of mercury) and auricular fibrillation, with an average heart rate of 120 per minute at the apex beat. The symptoms of cardiac failure had been present for over a year and he had been in hospital six weeks previously under medical care.

For the past month he had suffered from repeated bouts of gnawing epigastric pain which would come on at any time but, he thought, more often soon after meals; it was, however, unrelated to exertion. No other abdominal symptom was present.

On examination of his abdomen there was a large firm mass below the right costal margin, extending almost to the level of the umbilicus and continuous with the liver which was just palpable laterally. This mass had a distinct regular margin; it moved freely with respiration and was slightly tender. It was dull to percussion and was not palpable bimanually from the loin.

The usual medical treatment for the cardiac condition was instituted, comprising oxygen therapy, digitalization and mercurial diuretics. Resting in bed, the patient was soon noticeably less distressed, but the gnawing epigastric pain persisted with varying intensity.

For three weeks the patient remained in bed without further improvement; he then had a more severe attack of epigastric pain and vomited. On abdominal examination at this time there was mild general distension but the mass previously noted below the right costal margin was no longer palpable. The vomiting and the distension increased over the next two days and he died with the added signs of bronchopneumonia.



Photograph of autopsy specimens. The inferior surface of the liver is seen with a large open cavity in the right lobe. This cavity is lined by fibrous tissue and is the site of origin of the hydatid cyst which is seen below. The cyst measured five inches in diameter.

At autopsy

On opening the abdomen it was at once apparent that a mild general peritonitis was present. Along the right paracolic region extending from the inferior surface of the liver right down into the pelvis there were fibrinous adhesions between the loops of small bowel which were lying in front of the caecum and colon. There were also adhesions holding the ileum firmly in the pelvis. When these last were broken away—a simple matter—there was found in the pelvis and overlying the bladder, a rounded cyst typical of a hydatid. This measured some five inches in diameter and showed no

attachment to any surrounding structure. Later, a defect in the liver was found which appeared to have been the site of origin of the hydatid.

The remainder of the peritoneal cavity showed recent acute inflammation of a very mild type. The fluid was only slightly bile-stained.

The liver showed a large fibrous-walled cavity situated on the right side in the lower free margin and extending into the lower surface. This was partly obliterated by recent adhesions. The rest of the liver was free from cysts, but there were advanced parenchymal changes due to chronic venous congestion.

The spleen was firm. The gastro-intestinal tract from oesophagus to rectum showed no internal abnormalities of note; however, there were inflammatory changes of different degree in different parts of the outer coats.

There were small effusions in both sides of the pleural cavity, and in each lung there were two or more recent infarcts in the lower free borders. Pulmonary venous congestion was intense but there was no consolidation of inflammatory type.

The heart and pericardium were normal from the exterior. There was considerable hypertrophy of the left ventricle; the coronary arteries were grossly atheromatous.

DISCUSSION

The cause of rupture of this hydatid cyst, as with most, is obscure. Only rarely has there been a definite traumatic episode such as a blow from a cricket ball or a fall against a solid object. Sometimes leakage has clearly followed surgical aspiration. In most cases the cause is not found although, as in this man, the increased respiratory movements of the diaphragm and abdominal muscles required in the dyspnoea due to his cardiac failure possibly played a part. The altered state of the liver due to the chronic venous congestion may have been a contributing factor by interfering with the state of nutrition of the adventitia.

From the history of gnawing epigastric pain, present for weeks previously with a sudden exacerbation at the time of clinical rupture, it is clear that the process of adventitial tearing in this man was not rapid. However, there was nothing at autopsy to reveal the sequence of changes during extrusion of the cyst. The fibrous adventitia covering the free lower surface of the cyst, when this was still in the liver, must have given way gradually over the previous month, the changes in tissue tension probably producing the dull, gnawing epigastric pain. Finally, while he was at rest in bed, there was tearing of the last layer of the adventitia and the tense cyst was protruded by the respiratory excursion into the defect thus produced. The elastic properties of the intact laminated membrane allow extrusion through an adventitial rupture with, when free, resumption of the spherical shape.

The phenomenon of rupture of the adventitia only, with extrusion of the intact cyst into the peritoneal cavity, is less common in adults than in children where the adventitia is thinner (Dew, 1928). The commoner forms, seen in adults, of rupture of hepatic hydatid cysts are those involving all layers of the cyst wall and resulting in the spilling of cyst contents into the peritoneal cavity. Peritoneal rupture of the alveolar form of liver hydatid cysts is very rare (Neugebauer, 1933).

In cases of complete rupture, apart from a few cases where rupture has followed direct trauma, it is usual to find that the cyst is complicated in some way before the event. A previous small breach in the laminated membrane is common and in these cases, on rupture, the resulting daughter cysts are liberated. Escape of bile-contaminated fluid from the mother-cyst, or the leakage of bile from the wall of the adventitial cavity after cyst rupture, results in a choleperitoneum.

The fate of the mother-cyst cavity in the liver after complete rupture depends on whether the elastic laminated membrane has produced the complete extrusion of all hydatid elements, in which case the remaining adventitial space will become obliterated by organization of the blood clot and bile which has leaked into it from its walls. The cavity left after extrusion of the intact cyst is obliterated by the same process of granulation over the following weeks. If parts of the ruptured cyst are retained they may survive and refill the cavity with daughter cysts; or may die and remain as an inspissated necrotic mass finally becoming calcified; or may become infected, which is an uncommon but dangerous complication.

In the closure of the liver cavity after rupture of a hydatid cyst, the role of the adventitia is paramount, and, as emphasized by Curutchet (1948), the effective closure may be interfered with by calcification or infection of this layer.

The changes in the peritoneal cavity on complete rupture of liver hydatid cysts differ from those when an unruptured cyst is extruded. In the second case there are mild inflammatory changes in the region of the cyst producing filmy adhesions as were present in the case under discussion. The main changes in this case are due to coincident loss of blood or bile from the adventitial cavity whose fibrous lining is now laid bare. Such an implanted cyst will survive by diffusion of nutriment across the laminated membrane from the peritoneal fluid (Piaggio Blanco, 1946). When there has been complete rupture of the laminated membrane of the liver cyst, the hydatid fluid, with its contained daughter cysts or brood capsules and scolices, is released and there is the likelihood of the survival and growth of many of these fertile elements, resulting in multiple secondary peritoneal hydatid cysts. This is the usual route of infestation of the peritoneal cavity. Even a small leakage, producing so few symptoms as to be unnoticed or forgotten by the patient, is enough to produce extensive peritoneal sowing (Barnett, 1941).

The release of a large amount of hydatid fluid, particularly if bile leakage occurs at the same time, produces the clinical features of ascites. This fluid becomes walled off by a soft fibrinous membrane which is deposited over the surface of the abdominal viscera. The stomach and small bowel usually form the posterior wall of the space and in the production of the vascular membrane Dévé (1917) has stressed the role of the bile present.

Del Campo (1927) and Prat (1930) have thrown considerable doubt on Dévé's theory that bile is the main factor in the production of the encysting membrane by demonstrating its production in cases where no bile leakage has occurred. Dévé (1931) met this challenge by reporting a case of traumatic rupture of the left hepatic duct with choleperitoneum and death after four weeks in which the typical membrane enclosed the large biliary collection.

Pérez Fontana (1946, a) demonstrated the presence of degenerated hydatid elements in the membrane. These were surrounded by a foreign-body reaction similar to that which occurs elsewhere in the body on death of scolices and daughter cysts (Bacaloglu *et alii*, 1929; Hueston, 1952) and he ascribes the main provocative role in the formation of the encysting membrane to the released hydatid elements rather than to the bile present. This was supported by the production of typical membrane following inoculation of hydatid fluid with scolices into the peritoneal cavity of rabbits (Pérez Fontana, 1946, b) and by such case reports as that by Mazzini and Brachetto-Brian (1932) where typical membrane was formed without the presence of bile.

The conclusion at which one is compelled to arrive is that the sudden introduction of a volume of irritant material, whether bile or hydatid fluid, into the peritoneal cavity will give a "membrane" so that the fluid will be walled off by fibrinous adhesions until it is resorbed. If this is a slow process, organization of the adhesions will occur from subserosal vessels and produce a vascular membrane. The inclusion of bile or hydatid elements in this membrane shows the nature of the irritant, but in the case of a ruptured hydatid cyst of the liver both factors will play a part (Chifflet and Ardao, 1935).

The relative importance of each factor will vary in different cases. In the present case, where there has been no leakage of hydatid fluid, the peritoneal changes have been directly due to the liberation of a small amount of bile and blood from the adventitia. When there is no such leakage, there are minimal changes in the serosal coat and the cyst remains quite free in the pelvis as in the case reported by Allen (1882).

On drainage of an encysted hydatid effusion, no matter how massive, resolution of the serosal changes occurs and the peritoneal cavity may return completely to normal (Robb, 1945). The case reported by Barnett (1927), with enormous abdominal distension due to multiple peritoneal hydatid cysts, showed a dense membrane binding the abdominal viscera to the posterior abdominal wall. However, Barnett reports later (1944) that, on removal of two recurrent cysts seventeen years later, the peritoneal cavity was clear and the viscera were free and mobile. This phenomenon, observed in various parts of the body but especially in the serosal cavities, is an expression of the capacity of tissues to return to the normal or mean when unusual stimuli disappear.

The general changes in the body will also differ when the cyst remains intact, and again the difference depends on the absence of hydatid fluid leakage as in this case. There are not the anaphylactic phenomena nor the eosinophilia which are both significant in most cases of sudden complete cyst-wall rupture (Graham, 1891).

Diagnosis

Pre-operatively, it is almost impossible to diagnose the extrusion of an intact hydatid cyst of the liver. Thus, in the case of Orihuela (1935), the diagnosis of acute appendicitis was made and, in fact, the clinical features will be different in different cases and prohibit any accurate diagnosis. However, in the present case there was an opportunity such as few physicians are offered of making a correct pre-operative diagnosis. There was a large palpable mass attached to the liver when the patient arrived in hospital; later, after the clinical collapse which occurred while he was at rest in bed, the case history notes record that the mass was no longer palpable. Here the severity of his myocardial disease, resulting from arteriosclerosis, had so coloured his previous illness that the significance of the abdominal findings was not appreciated and the collapse was attributed to coronary insufficiency.

The anaphylactic phenomena of rash, shock and bronchospasm will be seen only in those cases where leakage of hydatid fluid occurs (Mussio-Fournier and Seoane 1927) and hence are not seen with intact cyst extrusion.

When the extrusion has been so slow as to produce few symptoms and the patient has survived, the cyst, surviving by diffusion from its new serosal surroundings, will only be found later in a clinical or autopsy examination of the pelvis or omentum, wherever implantation has occurred. The occurrence of pedunculated cysts from the liver as mentioned by Arce (1941) is probably explained by a similar slow extrusion of a superficial liver cyst which is then retained by the visceral layer of peritoneum or by local fibrinous adhesions.

The phenomenon of a solitary pelvic hydatid cyst with no hepatic cyst, such as reported by Penington (1937), is seen after a latent period of months or years following liver extrusion. However, the growth of pelvic cysts is more commonly from daughter cysts or scolices liberated on leakage of an hepatic cyst. The difficulties in diagnosis of pelvic hydatid cysts are notorious, for they may simulate bladder (Nisio, 1950), rectal, ovarian (Burmester, 1949) and even prostatic (Gompan, 1928; Battista, 1930) disease.

SUMMARY

(1) A case is recorded in which a hydatid cyst of the liver was extruded intact from its fibrous adventitia and, at autopsy, was found loose in the pelvis.

(2) The mechanisms of rupture and subsequent survival of the cyst are discussed and compared with those of cysts in which complete rupture of the wall with escape of contents occurs.

(3) The absence of hydatid fluid leakage from an intact cyst will greatly modify the prognosis.

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CASE REPORT

A CASE OF PRIMARY ABDOMINAL PREGNANCY

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Adelaide

THE current opinion about primary abdominal pregnancy was well summarized by Novak (1947) when he said: "While the possibility of primary abdominal pregnancy has been discussed for many years and while a very small number of purported instances have been reported, the majority of authors have questioned its possibility." It seems, therefore, justified to publish, in brief, the notes of a case which, in our opinion, fulfils the criteria of a primary abdominal pregnancy.

Clinical History

Mrs. S., aged 31 years, when seen by one of us (R.D.C.), complained of severe lower abdominal pain of about four hours duration. Her initial symptom was pain in the perineum and in the lumbar region of the back, with a feeling of cold at 8 a.m. After going to bed, she had become dizzy if she sat up. Her general health had been excellent. She had one child aged 4 years 7 months, which had been delivered without complications. There was no history of any miscarriages; precautions had been taken against pregnancy since the birth of the first child. Her menstrual periods were regular, every twenty-eight days; the last period was twenty-seven days previously, at which a normal loss had occurred at the normally expected time and for her usual five days. The next period was due the following day.

On examination, she was very pale and obviously in pain. Her pulse was rapid with poor volume. The lower abdomen was acutely tender with diminished respiratory movements. Rebound tenderness was marked and muscle guarding present. Pelvic examination revealed normal external genitalia and acute tenderness in all fornices and on movement of the cervix. No mass was palpable.

Thus, clinically, the patient presented a picture of an intra-abdominal haemorrhage, and a provisional diagnosis of a ruptured ectopic pregnancy was made, even in the absence of any missed period.

At operation, the peritoneal cavity was found to be full of blood and blood clot, particularly in the pelvis. However, on inspection of both tubes and ovaries, no abnormality was found. It was then noticed that a bleeding point was present on the lower part of the greater omentum which had been delivered from the pelvis without difficulty or the division of any adhesions. On closer inspection, it was noticed that the bleeding (now only slight) was coming from what appeared to be a small hole in a haematoma about 1.5 cm. in diameter. This area was excised, the peritoneal cavity cleared, and, as no other bleeding point could be seen, the abdomen was closed.

The patient made an uncomplicated recovery without blood transfusion and was discharged on the 19th day.

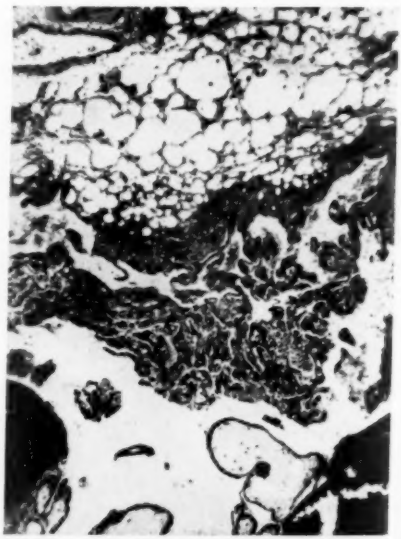

FIG. I. Photomicrograph of part of the wall of the haematoma, showing the anchoring of the trophoblast on the omental fat tissue and a few chorionic villi. (x 30)

Pathological Findings

The omental mass appeared to be a rounded haematoma and measured 1.5 x 0.9 cm. when cut across for section.

Microscopically, the lesion consists of a mass of blood clot with chorionic villi scattered throughout. The villi are mainly well preserved though some are necrotic and they are of all sizes up to a millimetre or so in diameter. Some villi show the hydropic degeneration of the stroma and scantiness of blood vessels which one often sees in the early stages of a hydatidiform mole. The trophoblast shows distinct Langhans and syncytial layers, with syncytial budding. There is some localized proliferation of the trophoblast, but this is not more extensive than it is usually seen in normal early placentation (Figs. I and II).

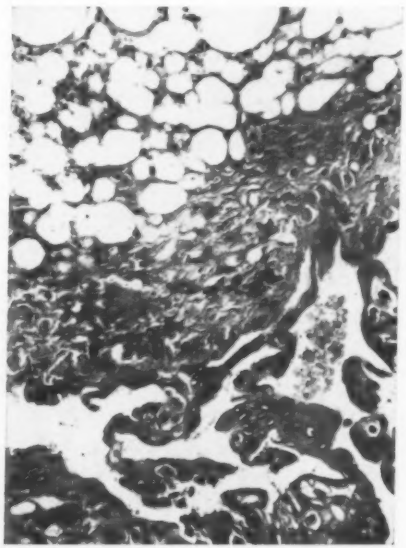

FIG. II. Photomicrograph of central area of Fig. I under higher magnification. Details of the anchoring trophoblast and the reaction of the fat tissue are shown. (x 110)

Between the extravasated blood and villi, and the fat of the omentum is a zone of fibrin, young connective tissue and lymphocytic infiltration, the different elements occurring in varying proportions. Embedded in this zone, and extending into the surrounding fat for a variable distance up to 2 mm., are circular bodies, staining pink in the haematoxylin and eosin section. Many have a concentric layered structure, and they vary in diameter from 9μ to 66μ. Some are in clusters and are then associated with epithelial cells. All stages from pink necrosis to cellular forms resembling trophoblast are seen, and they appear to represent outlying invading, trophoblastic elements, possibly even small villi, which in the unfavourable nidus of the fatty tissue of the omentum, instead of uterine muscle, have necrosed. As in normal pregnancy they appear to be mainly syncytial in origin (Fig. III).

No evidence of decidua formation is seen. Some cells at the periphery, lining the surrounding fat, with some resemblance to decidual cells, are Langhans cells with associated syncytial buds.

No trace of the embryo was found in the sections. It was probably extruded with the blood into the peritoneal cavity and lost.

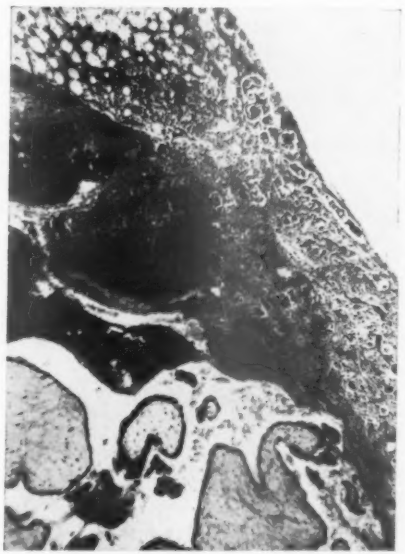

FIG. III. Photomicrograph of part of the wall of the haematoma, showing, apart from some chorionic villi, the inflammatory infiltration of the fat tissue and the spherical bodies described in the text. (x 30)

DISCUSSION

An examination of the literature on abdominal pregnancy shows that there have been quite numerous reports on this condition in the last few decades. A very careful review of the literature by Beacham and

Beacham in 1945 lists 185 papers and refers to over 300 cases. By far the majority of these reports, however, deal with pregnancies which had advanced into the second half of the normal gestation period or even beyond term. Amongst them, there is an Australian observation by Moore (1948). The main point of interest in these papers is usually the management of the obstetric difficulties, and most of the reported cases are obviously cases of secondary abdominal pregnancy. The number of reports on very early, and undoubtedly primary, abdominal pregnancies has remained very small indeed. Lindemann (1949), who described a case very similar to our own, states that most of these few cases show the site of nidation to be some part of the pouch of Douglas; he gives references to other cases, in which the implantation had occurred near the liver or on the spleen, but believes that an omental pregnancy had been described only once before. Studdiford, who recorded a primary abdominal pregnancy with implantation on the posterior surface of the uterus has laid down the criteria which have to be met before an abdominal pregnancy can be recognized as primary. They are:—

(1) both tubes and ovaries to be normal with no evidence of remote or recent injury,

(2) absence of any utero-peritoneal fistula,

(3) the presence of a pregnancy related exclusively to the peritoneal surface and young enough to eliminate the possibility of secondary implantation from a primary nidation in the tube.

The case discussed above meets these criteria to the full extent, it contributes to allaying the doubts so often voiced in the literature about the occurrence of true primary abdominal pregnancies and is in addition an example of the extremely rare primary nidation of the ovum in the omentum.

ACKNOWLEDGEMENTS

We wish to thank Dr. H. F. Bettinger, Director of Pathology, The Women's Hospital, Melbourne, for his advice in the preparation of this paper and the Photographic Section of his Department for the photomicrographs.

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Books Reviewed.

A SYNOPSIS OF OPHTHALMOLOGY.

By J. L. C. MARTIN-DOYLE, M.R.C.S., L.R.C.P., D.O. Bristol: John Wright and Sons Ltd., 1951. 7¼" x 4¾", viii plus 238 pp. Price: 20s.

Anybody who sets out to write a synopsis of ophthalmology must command our respect for his courage and excite our sympathy for the difficulties he will encounter in the matter of selection. This is the more true when the book is designed, not only for "the senior student" and "the busy general practitioner," but also for the "post-graduate student sitting for his Diploma." The author has overcome this difficulty in large measure by writing fully of the commoner conditions and cursorily of the rarer lesions. But his attempt to cater for such a wide clientele has led, at times, to a certain lack of balance, notably in the chapter on the lens where he devotes considerable space to the bio-chemistry of the lens and omits to mention dislocations of that body, their diagnosis and treatment. There are some other rather surprising omissions; the use of the plane mirror at 1 metre as a first step in examination of the fundus; of vaseline after carbolization of corneal ulcer; of Placido's disc in the diagnosis of conical cornea; any mention of spasm of the inferior oblique muscle and of penicillin in the treatment of *ophthalmia neonatorum*.

There are also some errors in proof-reading. On page 43, the pupil is described as "a round *diaphragm*"; on page 173, the latter half of the sixth line should read "the *left* eye tries to look," etc.; on page 175 the penultimate sentence of paragraph 1 should be "in the former case, it is a *di*vergent and in the latter case a *con*vergent squint." Other statements there are which will not receive universal acceptance such as the use of posterior sclerotomy for iritis with raised tension (paracentesis through the cornea is not even mentioned); that rupture of the choroid is "rare except as a war-time blast injury"; that the magnet should be used before an intra-ocular foreign body is localised by X-ray; that prisms are of use in paralytic squint and that information as to the nature of a melanoma of the iris should be sought by "removing a nodule by iridectomy for microscopical examination." His reference on page 112 to lamellar cataract occurring "most commonly of all in children whose mothers suffered from rubella in the very early stages of pregnancy" appears to be due to confusion in the author's mind between lamellar cataract and "Gregg's Cataract," two very different things.

Despite these criticisms, most of which can be eliminated in future editions, the book will find a ready use and meet a definite need. The various lesions are arranged systematically under their appropriate headings. The information it contains is clearly and concisely set out and easily found. The facts are right up-to-date and the chapters dealing with recent developments are particularly good. A table setting out the characteristics of the various syndromes is of particular value to the post-graduate student.

Taken all in all, it is a useful book, the main drawbacks of which are those inherent in any "synopsis."

ESSENTIALS OF NEUROSURGERY.

By LESLIE C. OLIVER, F.R.C.S. First Edition. London: H. K. Lewis and Co. Ltd., 1952. 8½" x 5½", viii plus 198 pp., 50 illustrations. Price 25s.

In his preface the author says that the book is intended as a guide to neurosurgeons in training and candidates reading for higher examinations.

Its scope is certainly not greater than this. Quite skilfully it consolidates in tabloid form the principles and practice of neurosurgery in the limited sense of surgery of the central nervous system. It could never serve as a book of reference or guidance in neurosurgical problems, and for this reason together with its complete lack of any bibliography, would be of most limited value to a neurosurgeon in any degree of advanced training.

For the higher examination it could take its stand with such masterpieces of consolidation as Love's "Shorter Surgery" — which is clearly the model.

A curious departure from the general tone and object of the book is a whole chapter written as personal experience devoted to the surgery of Parkinsonism, a disproportionate tribute to a somewhat unpromising surgical experiment.

THE QUIET ART. A Doctor's Anthology.

Compiled by Dr. ROBERT COOPE. Edinburgh and London: E. & S. Livingstone Ltd., 1952. 7½" x 4¾", xii plus 284 pp., frontispiece. Price: 12s. 6d.

Dr. Robert Coope has collected together in this volume a delightful series of extracts by and about doctors. The garden from which he has collected his flowers is a large one, covering as it does all aspects of literature. There is humour, pathos and deep understanding of the way of life in the extracts skilfully collected and arranged by the compiler. The book is one which can be repeatedly taken up and read.

THE LIFE AND WORK OF ASTLEY COOPER.

By R. C. BROCK, M.S., F.R.C.S., F.A.C.S. Edinburgh: E. and S. Livingstone Ltd., 1952. 9" x 6½", viii plus 176 pp., portrait and 14 plates. Price: 20s. stg.

Mr. R. C. Brock, of Guy's Hospital, well known to surgeons for his work on the anatomy of the bronchial tree and the surgery of pulmonary abscess has produced a delightful biography of Sir Astley Paston Cooper one of the most famous of Guy's surgeons. This work was originally planned in 1941 as a fitting memorial to Cooper on the occasion of the centenary of his death, and it is unfortunate that the printing of the book has been delayed until now. It is only proper that the book should have been written by a surgeon of the Hospital which Cooper adorned and for which he did so much. As the author points out in the preface, Cooper has received scanty notice throughout the years and although his biography

was published in 1843 by his nephew, Bransby Cooper, it is important that Cooper's place in the history of surgery should be assessed in retrospect and this is admirably done in the present volume.

Cooper was the last of the great surgeon-anatomists of the eighteenth and early nineteenth centuries and had he not immediately followed the great John Hunter would have made a far greater place for himself in the history of surgery. His books on the anatomy of hernia and the breast are classics and can be studied with profit to-day.

Brock's biography is excellent and gives a clear picture of the man and his many-sided interests and to those who wish to get an idea of the state of surgical knowledge early in the last century this book can be thoroughly recommended.

DISEASES OF THE NOSE, THROAT AND EAR.

By I. SIMSON HALL, M.B., Ch.B., F.R.C.P.E., F.R.C.S.E. Fifth Edition. Edinburgh: E. & S. Livingstone Ltd., 1952. 7½" x 5", xii plus 463 pp., 82 illustrations plus 8 coloured plates. Price 18s. net.

The appearance of a fifth edition is a sufficient tribute to the use and popularity of this well known book with students and practitioners alike. A reading of the text convinces one that most modern advances have been noted and recorded.

There is room, however, for a much more drastic revision of outlook and technical methods, e.g., in local anaesthesia surely nasal packing is now outmoded and, if in other treatments, ribbon gauze is to be packed into the nose its careful preparation with emollients or lubricants should be stressed.

For the student a rather more didactic approach to the use of antibiotics would seem advisable especially emphasizing the necessity for prolonged administration in the case of acute otitis—acute sinusitus, etc.

A realistic reconsideration of formulae given in the appendix would be helpful and in particular the use of modern bases for ointments should be incorporated since they so greatly increase the therapeutic effectiveness of the drugs used.

Despite these criticisms the book is to be highly recommended.

CLINICAL RADIOLOGY OF THE EAR, NOSE AND THROAT.

By ERIC SAMUEL. First Edition. London: H. K. Lewis and Co. Ltd., 1952. 10" x 7½", viii plus 339 pp., 320 illustrations. Price: 70s. net.

With the increase in specialization it is inevitable that there shall be some degree of fragmentation in so large a specialty as is radiology and it can be said immediately that the book deserves the warmest welcome from all interested in oto-rhino-laryngology.

There is a division, as one would expect, into the three component parts of the specialty and in each instance the survey of the section, both as to letterpress and illustration, is as full and adequate as could be wished for. It is difficult to think of any serious omissions and the list of references given at the end of each chapter is extremely valuable.

The reproduction of the films is beyond all praise: a uniformly excellent level of clarity has been attained despite the fact that nearly all the illustrations seem to have been specially prepared for the book.

Having said so much in praise it is regrettable to have to say that proof reading has left many errors; that the lettering and key to some of the diagrams (e.g., page 269) seems to have been placed in the hands of the office boy. There is also serious confusion in describing the various types of mastoid operation and this should be corrected in subsequent editions. Concerning this point, it is as well to say that too much should not, as in this instance, be attempted by the radiologist: clinical examination will determine far more accurately what the surgeon wants to know: X-ray films can be but a minor contribution to the solution of his problems.

These, however, are minor blemishes and the book demands a place on the book shelf of every ear, nose and throat specialist.

PATHOLOGY OF THE CELL.

By G. R. CAMERON, M.B., D.Sc., F.R.C.P., F.R.S. Edinburgh: Oliver and Boyd Ltd., 1952. 10" x 6½", xv plus 840 pp., 41 figures, 64 plates. Price: £4 4s.

In a generation in which it is generally accepted that the cell is the biological unit, a book which deals exhaustively and authoritatively with the subject must be of importance to everyone. This volume provides this and thus will be the standard work on the subject for some considerable time.

As is clear from the dedication, Professor Cameron is an Australian who was educated in Melbourne. Indeed, he was Sir Harry Allen's last Stewart Lecturer in the Department of Pathology. Subsequently he was associated with Aschoff and, since then, has occupied various positions in schools in Great Britain. Now, as the Professor of Pathology at University College Hospital Medical School, he is a thoroughly appropriate person to present this work and his Australian colleagues have reason to be proud of him.

This book is divided into four parts, the first of which deals with the normal cell, the second with the abnormal cell, the third provides a critical discussion of the cell theory and the fourth embodies the author's prognosis for developments in the field of cytology.

The first part presents the history of our knowledge of tissues from the point of view of the cell and the development of the cell theory. Like other parts of the book, it is dealt with in a broad manner which will be interesting as well as instructive to those who are not necessarily primarily interested in cytology. There is here, also, a consideration of various philosophical propositions; for example, there is an excellent chapter devoted to Teleology. At the same time there is a great deal of precise and detailed information regarding all the aspects of the cell.

In the second part there is a general consideration of the various abnormal conditions covering an extremely large field. There is a study of the

development of the cellular theory in pathology and, in addition, there is consideration of all the various changes (degeneration, necrosis, atrophy, hypertrophy, regeneration, *etcetera*) in various circumstances. Observations on isolated cells and on cells as they occur in the tissues are discussed. The problems relating to the growth of transplanted cells are considered and there is a chapter on the plant cell.

The third part deals with criticisms of the cell theory and these are discussed from the point of view of embryology, morphology and functional studies.

The fourth part contains an excellent account of recent work that has been done with new techniques such as electron microscopy, X-ray crystallography and the like. This will be of great value to the advanced student.

In general this book is a mine of information. It is not primarily a book for the undergraduate but rather one for the post-graduate and for the investigator. It will be found to be an excellent work of reference. At the same time it will be found also very useful as a reference book for the student.

There is a very large bibliography containing many references which would not ordinarily be encountered. It is clearly the result of prolonged attention to the problems and has been compiled by a keen student and a master of the subject.

The general production of the book is of high standard. The illustrations are good and it is not an overstatement to describe some of them as magnificent. There is a satisfactory general and author's index.

This book can be strongly recommended to everyone who has an interest, from any point of view, in pathology.

WILLIAM SMELLIE, THE MASTER OF BRITISH MIDWIFERY.

By R. W. JOHNSTONE, C.B.E., M.A., M.D., Hon.LL.D. Edinburgh: E. and S. Livingstone Ltd. 9" x 6½", viii plus 139 pp., frontispiece and 30 plates. Price: 21s. stg.

It is sixty years since the last authoritative biography of one of the greatest British masters of midwifery was written by Professor Glaister, and this volume has long since been out of print. A new biography with an assessment of Smellie's position in the history of obstetrics has long been overdue, and this has now appeared written by the Professor-Emeritus of Midwifery at the University of Edinburgh. Professor Johnstone has given a delightful account of Smellie's life and, in particular, a critical analysis of his writings. It is a remarkable fact that details of Smellie's life are extremely meagre, but since Glaister's book was written two important sets of documents have come to light. One is the travel journal of Dr. Peter Camper with much detail as to Smellie's method of teaching and the second is some manuscript autobiographical material written by Smellie in the Hunterian Library at Glasgow. This new material is adequately dealt with by Professor Johnstone; the Smellie letters being reproduced in facsimile in the book.

Professor Johnstone is to be congratulated on producing this excellent account of Smellie's work and his struggle to improve, by his teaching, the standard of British midwifery. Midwifery to-day owes more than it can repay to Smellie and he can truly be called the Master.

THE ENGLISH PIONEERS OF ANAESTHESIA.

By F. F. CARTWRIGHT. Bristol: John Wright and Sons Ltd., 1952. 8¾" x 5½", x plus 338 pp., 18 plates. Price: 21s. net.

Much has been written of the early clinical use of anaesthetics and little material has been collected of the spade work which made this clinical application possible.

The author of this admirable volume has given us an attractive history of the pioneer work performed in England prior to the performance of painless surgery.

When one considers that Priestly discovered nitrous-oxide in 1773, it is rather tantalizing and surprising that it was not until 1844 that Morton used it for surgery, especially as Davy administered it so often to himself in sub-anaesthetic doses.

The book consists of 3 short biographies: J. Thomas Beddoes and his pneumatic medical institute, Humphrey Davy and Henry Hickman. Little is known of the latter beyond his ambition to relieve the pain of surgery which he did in animal experiments with carbon dioxide. Of the other two, Beddoes and Davy, he tells us much more and it is not only of anaesthetic interest but it is a sketch of English history at the close of the 18th Century. The lives of these men will interest all readers—their political activities and beliefs, their cultural associations with Wordsworth, Coleridge and Southey and their interest in chemistry and medicine.

These are pleasant, attractively written stories that should have a wide appeal not confined to the medical historian.

There are 330 pages of clear type with plates of historical interest.

Biographies and sources of information are quoted.

AN INTRODUCTION TO ABDOMINAL DIAGNOSIS.

By ALAN E. LEE. Sydney, N.S.W.: Australian Medical Publishing Co. Ltd., 1951. 9¾" x 6", 176 pp.

"An Introduction to Abdominal Diagnosis" is the title of a surgical handbook written by Alan E. Lee, senior visiting surgeon of the Brisbane Hospital.

The medical profession will welcome this book because the author has chosen a subject which is much in the mind of the scientific surgeon of to-day.

To appreciate the work, it is necessary to apprehend the author's thoughts. He feels that too many diagnoses are made by the negative process of elimination; that too much attention is paid to the absence of physical signs; that clinicians accept reports from radiologists, which are in fact clinical diagnoses, without considering whether the radiologist is competent to make such a responsible statement of surgical pathology. And above all he feels that the study of diagnosis as an application of inductive reasoning has been much neglected. It is to remedy this neglect that he has devoted his book "to the study of the nature of abdominal

symptoms with a view to enunciating an acceptable theory by which they may be related to their various causes."

The author analyzes abdominal sensations, the rationale of diffuse and local tenderness, and describes how pain depends on the adequacy of the stimulus in relation to the state of the pain threshold.

The greater part of the book is concerned with the study of the mechanism of symptoms and the significance of syndromes in diseases of the upper, mid, lower, and lateral abdominal regions. The author takes his readers through the processes of inductive reasoning in making a diagnosis in diseases particular to these regions; and explains the part disease factors play in moulding the symptoms and shaping the syndromes. These various minor theses are well argued.

In a book such as this there must necessarily be some weaknesses, for, owing to gaps in our knowledge of human physiology and to our limitations of knowledge of the intimate pathology of disease in living tissues, much of the reasoning in inductive diagnosis must be based on speculation or hypothesis—often a matter of opinion. But these are quite overshadowed by the strength of the book: by the boldness and soundness of its main theses, namely:— (a) that on a basis of present-day enlightened human physiology, the book gets down to the very heart of diagnostic art; to the inductive diagnostic reasoning of the pre-X-ray period, which produced the brilliant medical intellects of that period; (b) that it could well be an introduction to the diagnosis of the surgical clinical picture of the radiologist, which is in effect the representation, in terms of shadows, of pathological criteria in living tissue—a surgeon's job; and (c) that the book, in cultivating the art of inductive reasoning, must naturally develop in surgeons the art of deductive reasoning based on operation table findings in living pathology, in order correctively to oppose their inductive reasoning—a by-effect of which will be a constant enrichment of our diagnostic art as well as day-to-day additions to our knowledge of living pathology, and the result of which is that much of what in this book must be speculation or hypothesis will become elevated to accepted theory.

The book emanates from a mind rich in surgical experience, embodies a much needed directive in diagnosis, and cannot but be valuable to the working surgeon or the groping senior student.

The Australasian Medical Publishing Company is to be congratulated on an excellently produced book.

CANCER OF THE BREAST—A RE'IEW.

By D. W. SMITHERS, M.D., M.R.C.P., D.M.R.; P. RIGBY-JONES, M.B., D.M.R.; D. A. G. GALTON, M.B., B.Chir.; P. M. PAYNE, B.Sc. London: British Institute of Radiology, 1952. 9¼" x 7¼", 90 pp., 61 tables, 26 figures. Price: 20s.

At present well-established procedures in the treatment of cancer at common sites are being re-examined—often with useful scepticism. Studies of the life history of the developed disease are increasingly influencing the management of cases but much information still needs systematic collection and analysis.

Professor Smithers and some of his associates at the Royal Cancer Hospital, in this spirit of the time, have reviewed the records of all the patients (1777) who attended there in the period 1937-48 suffering from cancer of the breast. They have studied the more commonly asked questions about predisposing factors — those influencing prognosis and the results of treatment and finally have tried to arrive at a general policy for the selection of individual treatments. Their method is necessarily largely statistical but clarity is given by the free use of simple tables, graphs and diagrams. They show that there is a steady downward trend in the mortality rate, in England and Wales, after correction for age distribution of the female population.

Predisposing factors examined were heredity, social class and occupation, hormone balance, cystic hyperplasia, trauma, marital state and parity and breast feeding. In each case further information must be sought and to this end clearly focussed clinical histories are needed.

The section on prognosis is equally complete but it can fairly be summarized in their own words. "The most important factor in prognosis is the character of the tumour they develop," and this conclusion colours the whole of the discussion on treatment policy.

The critical discussion of methods of presenting results is illuminated by sentences like—"We believe everyone to be honest but know them to be biased"—and, after showing evidence of a widespread improvement in absolute five-year survival rates, often over-looked, they go on "We even reach the point when the best results yet put forward may come simultaneously from two centres with drastically opposing views."

The review is timely and should be of special value to teachers in its first part; and as a whole should stimulate re-examination of methods of treatment by those responsible for its choice.

Books Received.

TWENTY-FIFTH MEETING OF THE NORTHERN SURGICAL ASSOCIATION.

By Professor E. DAHL-IVERSEN, M.D. Copenhagen: Einar Munksgaard, 1951. 10" x 6¼", xv plus 460 pp. Price: 26s.

FRACTURES AND ORTHOPAEDIC SURGERY FOR NURSES AND PHYSIOTHERAPISTS.

By ATHUR NAYLOR, Ch.M., M.B., M.Sc., F.R.C.S. (Eng.), F.R.C.S.(Edin.). Third Edition. Edinburgh: E. and S. Livingstone Ltd., 1952. 8½" x 5½", xv plus 315 pp., 254 illustrations. Price: 22s. 6d. net.

TRAITÉ DE TECHNIQUE CHIRURGICALE. (Vol. II.)

By P. TRUFFERT. Paris: Masson et Cie, 1952. 9½" x 6½", 586 pp., 622 illustrations. Price: 4000 francs.

EMERGENCY SURGERY. Part IV.

By HAMILTON BAILEY, F.R.C.S., assisted by N. M. MATHESON, F.R.C.S. Sixth Edition. Bristol, England: John Wright and Sons Ltd., 1952. 6½" x 10", iv plus 139 pp., 311 illustrations, some in colour. Price: 21/-.

CLINICAL REPORTS.

Alfred Hospital. Melbourne: Brown, Prior, Anderson Pty. Ltd., 1951. 10" x 6¼", 84 pp., 23 illustrations.

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